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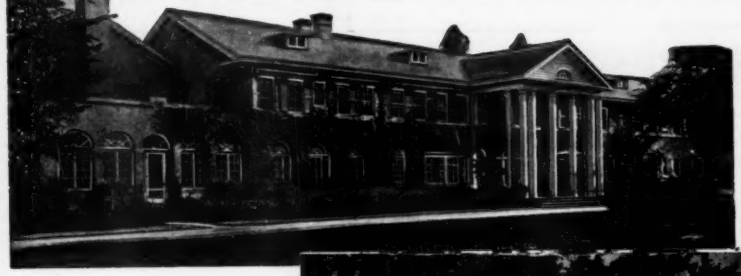

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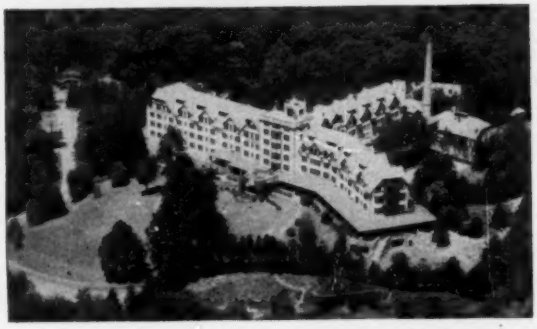

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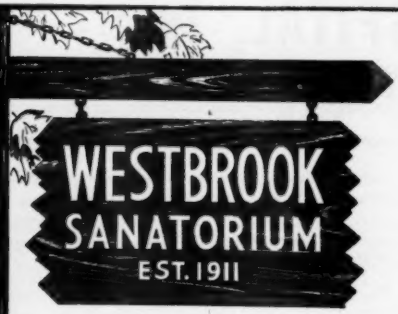

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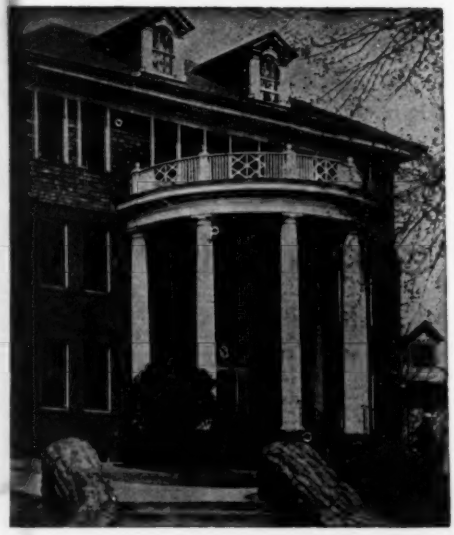

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POLIOMYELITIS

IV. A Study of the Midbrain

HOWARD A. MATZKE, Ph.D.
AND
A. B. BAKER, M.D.
MINNEAPOLIS

IN MANY cases of poliomyelitis the lesions are not limited to the spinal cord but extend throughout the nervous system, implicating primarily the brain stem. The lesions within the medulla are often very severe and have been studied and reported by many investigators. Recently we [1] have reported on the medullary changes in poliomyelitis and have succeeded in correlating pathological changes within certain cell groups with the clinical symptoms manifested by the patient. It was felt that other areas of the brain stem warranted detailed study. The present investigation consists of a serial study of the midbrain in cases of bulbar poliomyelitis.

The midbrain has received but scant attention in the various publications on this disease. In a number of cases of bulbar poliomyelitis one can be certain that the midbrain has been involved because of the presence of ocular signs. It is estimated that some ocular symptoms will be apparent in about 10 per cent of cases of bulbar poliomyelitis, even without a careful neurological examination. As early as 1905 Wickman [2] reported such involvement in 56 of 868 cases of poliomyelitis. Most patients had scattered oculomotor palsies, while in one case complete external ophthalmoplegia developed. Sautter,[3] in 1917, reported disturbances of the extraocular muscles in 3 per cent of 669 cases in an epidemic in Philadelphia. Thirteen patients had unilateral paralysis of the sixth nerve; ptosis occurred in one case, and nystagmus appeared

From the Division of Neurology, University of Minnesota Medical School.

This study was aided by a grant from the National Foundation for Infantile Paralysis.

1. Baker, A. B.; Matzke, H. A., and Brown, J. R.: Poliomyelitis: Bulbar Poliomyelitis; A Study of Medullary Function, Arch. Neurol. & Psychiat. **63**:257 (Feb.) 1950.

2. Wickman, I.: Studien über Poliomyelitis acuta: Zugleich ein Beitrag zur Kenntnis der Myelitis acuta, Arb. a. d. path. Inst. d. Univ. Helsingfors **1**:109, 1905.

3. Sautter, A. C.: Ocular Palsies in Infantile Paralysis: Report of 2 Cases, Tr. Coll. Physicians **39**:363, 1917.

in many. There were no pupillary abnormalities. In 1931 Nordmann and Duhamel [4] and Emmons [5] reported on the implication of the midbrain in poliomyelitis. Nordmann and Duhamel [4] observed a French outbreak and reported ocular symptoms in 19 of 60 cases. Pupillary difficulties appeared in only two cases. Emmons [5] checked 70 cases of poliomyelitis within two weeks of the onset of the illness and found ocular symptoms in 29 per cent. In 11 of these cases pupillary changes were present.

In most of the reported cases the chief symptoms referable to the midbrain consisted of ocular disturbances. A few scattered reports mentioned involvement of the substantia nigra with symptoms of parkinsonism. The most striking case was reported by Marinesco and associates,[6] in which a 1 year old child manifested trembling, hypertonia and hypokinesia two weeks after the onset of the flaccid paralysis of poliomyelitis. The symptoms of parkinsonism lasted three weeks. Vujic and Ristic [7] reported a case in which parkinsonism appeared two weeks after the onset of acute poliomyelitis and lasted ten days. The patient was followed for five years, without recurrence. Alajouanine and his co-workers [8] reported a case of a febrile illness which was followed in two or three months by typical parkinsonism. From the description of the acute illness one hesitates to accept this case as one of poliomyelitis. The condition could well have been epidemic encephalitis.

Pathological changes within the midbrain occur in poliomyelitis but have not received very intensive study. Perkins and Dudgeon,[9] in a case of bilateral ptosis and diplopia, observed diffuse cellular infiltration. Marinesco and associates [6] described the pathological changes in 28 cases. They felt that the changes could not be distinguished from those of epidemic encephalitis. In 15 cases vascular and intestinal lesions were observed within the substantia nigra. In most cases lesions were observed within the colliculi and the third nerve nuclei.

4. Nordmann, J., and Duhamel, E.: Lésions oculaires dans l'épidémie de poliomyélite du Bas-Rhin en 1930, Rev. franç. de pédiat. **7**:308, 1931.

5. Emmons, H. M.: Ocular Symptomatology in Acute Poliomyelitis, Am. J. Ophth. **14**:927, 1931.

6. Marinesco, G.; Draganescu, S., and Grigoresco, G.: Sur un cas de parkinsonisme postencéphalitique survenu chez un ancien poliomyélitique, Rev. neurol. **2**:102, 1929.

7. Vujic, V., and Ristic, V.: Le syndrome parkinsonien comme complication de la maladie de Heine-Medin, Presse méd. **46**:901, 1938.

8. Alajouanine, T.; Mignot, H., and Mozziconacci, P.: Un syndrome parkinsonien peut-il reconnaître la maladie de Heine-Medin comme étiologie? À propos d'un cas de poliomyélite antérieure aiguë avec narcolepsie, suivie peu après d'un syndrome parkinsonien, Rev. neurol. **72**:66, 1939.

9. Perkins, J. J., and Dudgeon, L. S.: A Case of Acute Poliomyelitis in an Adult with Marked Bulbar and Ocular Symptoms: Microscopical Report, Brain **30**:110, 1907.

Peters,[10] in 1938, described the pathological changes in 39 fatal cases of poliomyelitis. The predominant changes consisted of a severe mesodermal-glial infiltration in the region of the third nerve, the vegetative nuclear group and the substantia nigra. The last-mentioned structure was involved in 17 cases and showed not only infiltrative changes but also neuronal degeneration. Generally the author felt that the changes within the midbrain were not very severe or consistent.

PRESENT INVESTIGATION

The present study consists of a serial investigation of the midbrain of 111 patients dying of bulbar poliomyelitis in Minnesota during the period of 1946 to 1949. The sections were prepared with the Nissl stain, with hematoxylin and eosin and with the Weil stain. In a survey of this material, it became apparent that the midbrain in poliomyelitis contains two types of histopathological changes: (1) a diffuse interstitial cell reaction and (2) neuronal damage. In most cases both these changes were observed in varying degrees of severity. The interstitial cell reaction was by far the most striking but obviously of less significance clinically, since it was neuronal damage that ultimately determined the functional loss to the patient. Although these two changes occurred simultaneously within the midbrain, from the standpoint of simplicity they are better described separately.

INTERSTITIAL CELL INVOLVEMENT OF THE MIDBRAIN

The detailed histological nature of the interstitial reaction in poliomyelitis has received a great deal of study and has already been described and reviewed in detail by us in a previous publication.[1] The nature of this cellular reaction within the midbrain was similar to that of lesions within other areas of the brain stem and spinal cord. This interstitial cell reaction was present within the midbrain in every case of bulbar poliomyelitis and usually comprised the predominant tissue change. However, the intensity of these inflammatory alterations varied greatly from case to case and rarely was as severe as those seen within the medulla in the same case.[1]

Although the detailed histological nature of this interstitial cell reaction has been well documented, the distribution of these changes within the midbrain has not received any consideration in the literature. As would be expected, certain structures in the midbrain are much more involved than others. The severest involvement was always observed in the region of the tegmental nuclei situated in the dorsal and lateral

10. Peters, G.: Über den Ausbreitungsbereich des Krankheitsvorganges im Zentralnervensystem bei der Heine-Medinschen Krankheit, München. med. Wchnschr. **85**:1073, 1938.

regions of the midbrain (fig. 1). In these areas the mesodermal-glial reaction was comprised mostly of diffuse inflammatory elements, which varied from a few scattered cells to a fairly intense leukocytic infiltration. Only rarely was the inflammatory process so severe as to result in softening and fragmentation of the underlying tissues.

There was a sharp demarcation between the inflammatory reaction within the tegmental nuclei and the changes within the motor nuclei

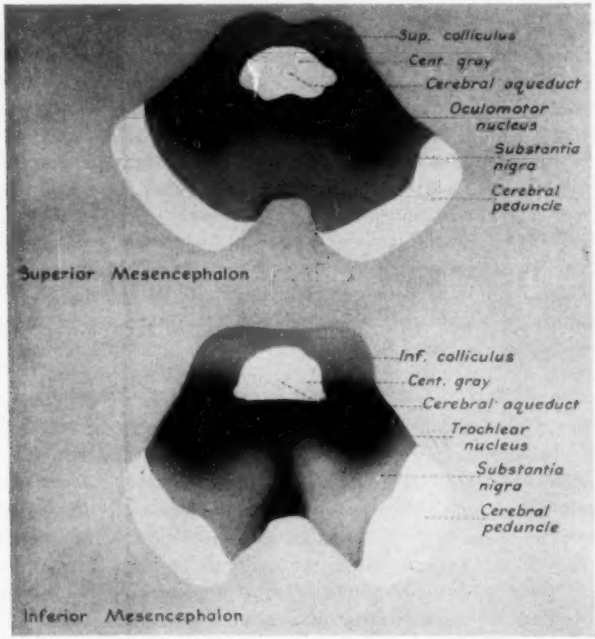


Fig. 1.—Intensity of the inflammatory reaction in the midbrain, as shown by the darkness of the shaded areas. In the superior mesencephalon the most intense reaction is in the lateral tegmental nucleus and the third nerve nuclei. In the inferior mesencephalon the severest inflammatory reaction is centered in the ventral, lateral and dorsal tegmental nuclei.

of the third and fourth cranial nerves. As a rule, the inflammatory reaction within the nuclei of these cranial nerves was less intense, this change occurring abruptly at the border of the nuclei. In spite of the fact that the over-all intensity of the inflammatory reaction within the nucleus of the oculomotor (third) nerve was less severe than in the surrounding tissue, the degree of involvement in the isolated case was

often much more marked. In a few cases this inflammatory reaction had produced severe softening and necrosis of the underlying tissue with complete destruction of the nucleus. This type of inflammatory necrosis within the oculomotor nucleus was observed in four cases, whereas it appeared within the tegmental nuclei in five cases and in the substantia nigra in but one case. There was a sharp discrepancy between the degree and intensity of inflammatory reaction within these motor nuclei and the severity of the neuronal damage. In most cases the inflammatory reaction was the more intense, the motor neurons often appearing structurally intact. However, in the occasional case the neuronal damage was very severe, in spite of a minimal degree of interstitial cell reaction.

The remaining structures within the midbrain, namely, the tectum, the red nucleus, the substantia nigra and the central gray matter, showed only very mild, and frequently no, interstitial cell involvement. Particular attention was given in our studies to the substantia nigra. In about 40 per cent of the cases this structure showed some inflammatory reaction, consisting primarily of focal lesions involving isolated clumps of neurons. Only rarely was the entire substantia nigra involved. Inflammatory changes were not observed within the cerebral peduncles in any of our cases of bulbar poliomyelitis. This is an interesting observation, since it corresponds closely with the absence of inflammatory changes within the pyramidal tracts of the medulla, as reported by us in a previous publication.[1]

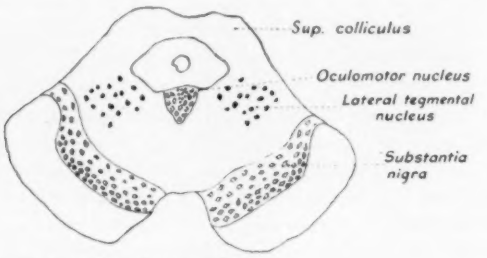
NEURONAL DAMAGE

From the standpoint of clinical symptomatology, the neuronal changes are by far the more important in this disease. In order better to understand the nature of such changes, it is imperative that one first have a fairly adequate knowledge of the normal cell groups within the midbrain.

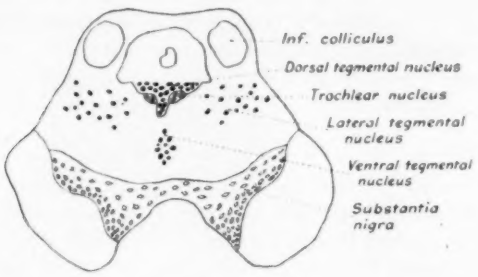
Normal Structure.—The nuclear groups in the midbrain consist of the nuclei (motor) of the third and fourth cranial nerves, the substantia nigra, the red nucleus, the colliculi and the tegmental nuclei. Since the colliculi and the red nucleus are little involved in bulbar poliomyelitis, they do not warrant detailed description at this time. By far the most important nuclear groups within this region are the tegmental nuclei, the motor nuclei of the cranial nerves and the substantia nigra (fig. 2). The motor nuclei of the cranial nerves are identical with the somatic motor neurons observed in the ventral horn of the spinal cord and have already been discussed extensively in the literature (fig. 3 *A*).

The substantia nigra extends throughout the length of the mesencephalon between the peduncle and the medial lemniscus. Its cells are arranged in a compact ventral layer and a scattered dorsal zone. On an

average the neurons of the substantia nigra are of the same general size and shape as the ventral horn cells of the spinal cord. However, they contain large accumulations of melanin, usually situated at one pole of the cell, with the cell nucleus displaced to the opposite pole. The Nissl substance, when present, is large and boxlike and confined to that half of the cell which does not contain pigment. The cells of the substantia nigra average about 42 by 24 microns in length and width, respectively.



Cell Groups of Superior Mesencephalon



Cell Groups of Inferior Mesencephalon

Fig. 2.—Distribution of the cell groups in the mesencephalon. The lateral tegmental nucleus is found throughout the extent of the midbrain, whereas the dorsal and ventral tegmental nuclei are confined to the inferior mesencephalon.

Many of the cells tend to be elongated, with the long axis directed horizontally (fig. 3 *B*).

The tegmental nuclei may be divided into three groups on the basis of position, size and arrangement of the cell groups, namely, dorsal, ventral and lateral tegmental nuclei (fig. 2).

Dorsal Tegmental Nucleus: This nuclear group is situated dorsal to the nucleus of the fourth cranial nerve in the lower mesencephalon. It is a small compact group of cells confined to the lower portion of the central gray matter and bordered laterally by the mesencephalic nucleus

of the fifth cranial nerve. It does not extend dorsally even to the central canal. A few cells are usually found wedged between the nuclei of the fourth cranial nerve. These cells are uniform in size and shape, measuring

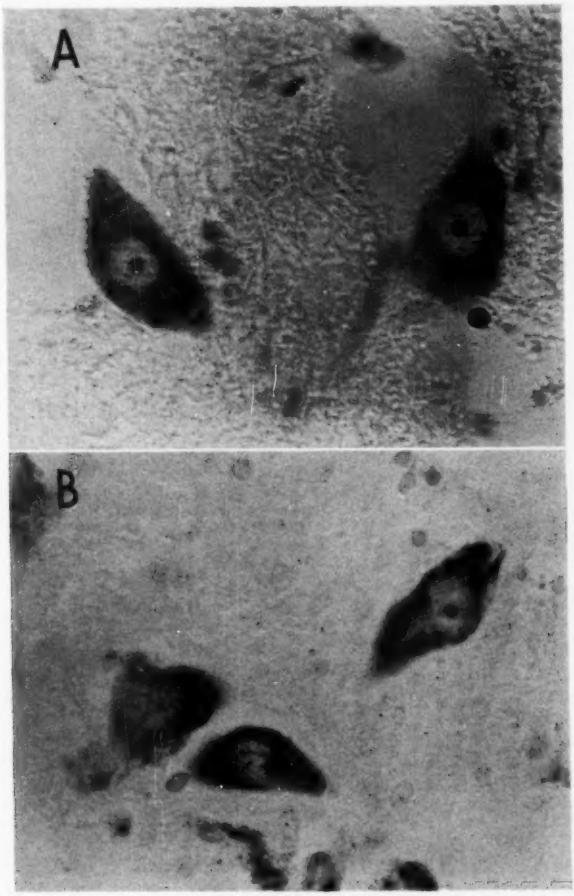


Fig. 3.—*A*, normal cells of the oculomotor nucleus. These cells are typical lower motor neurons. *B*, normal cells of the substantia nigra. Note the pigment, the large Nissl bodies and the eccentric nuclei. Nissl stain.

about 32 microns in length and 22 microns in width. They are usually oval, with a prominent nucleus and nucleolus. The nucleus is usually eccentrically placed. The Nissl substance is prominent, granular and

distributed evenly throughout the cell. The cell cytoplasm occasionally contains a brownish pigment which replaces the Nissl substance (fig. 4 *A*).

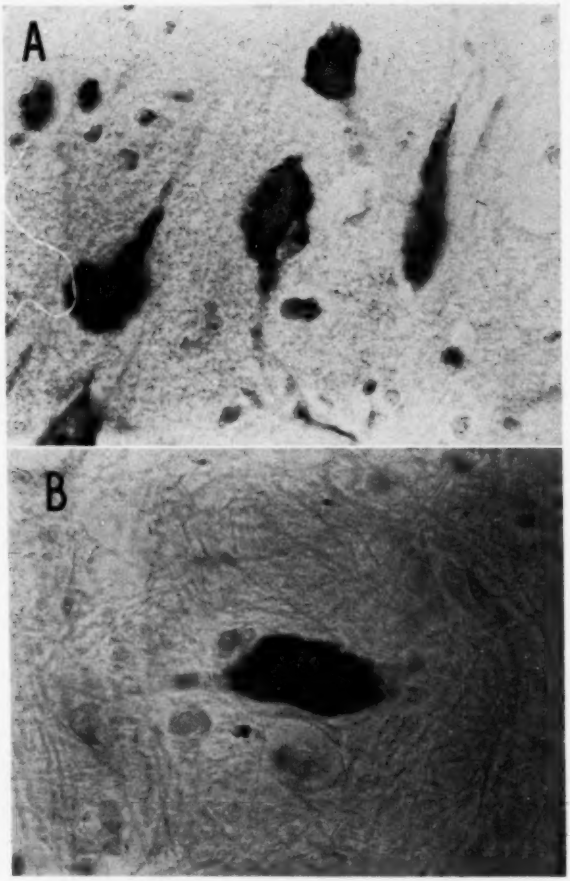


Fig. 4.—*A*, normal cells of the dorsal tegmental nucleus. Large accumulations of pigment displace the nucleus to the periphery. *B*, normal cell of the ventral tegmental nucleus. The heavy concentration of pigment often obscures the entire nucleus. Nissl stain.

Ventral Tegmental Nucleus: This is a small group of cells situated in the midline ventral to the dorsal tegmental nucleus. It is also limited

to the lower mesencephalon. The cells within this nucleus are loosely arranged and vary in size and shape. The cells average 33 microns in length and 17 microns in width. The largest are 50 by 25, and the smallest, 20 by 10 microns. These cells are usually elongated but may be oval. The nucleus is vesicular and eccentrically placed and contains a large, prominent nucleolus. The Nissl substance is finely granular and distributed uniformly throughout the cell. Pigment is very common and often replaces much of the Nissl substance, giving some of these cells the appearance of the cells of the substantia nigra and suggesting a relationship between these two structures (fig. 4 *B*).

Lateral Tegmental Nucleus: This is a large nuclear group extending throughout the entire mesencephalon. It is bounded by the tectum

Fig. 5.—Lateral tegmental nucleus. The neurons are small with finely granular Nissl substance. The nucleus is usually large and contains a distinct nucleolus. Nissl stain.

dorsally, by the red nucleus and the nuclei of the third and fourth cranial nerves medially and by the medial lemniscus ventrally. The cells are loosely arranged and vary in size and shape. The average cell is 22 microns long and 16 microns wide. The largest are 50 by 35 microns, and the smallest, 15 by 10 microns. They are usually polygonal but may be oval to elongated. The nucleus is large and prominent and contains a distinct nucleolus. The Nissl substance is granular, distinct and uniformly distributed (fig. 5).

Pathological Studies.—Because of the striking variation in the size and structure of the normal tegmental cells, great caution must be exerted in any study on the pathological alteration within these structures. Mild

changes, such as dissolution of the Nissl substance and eccentricity of the nuclei, cannot be relied on as definite evidence of cell injury. One must look for more extreme changes, such as cellular swelling, the formation of ghost cells, pyknosis of the cell or its nucleus, fragmentation of the cell or its processes or neuronophagia. In many cases structurally intact cells were invaded by phagocytes, indicating that the cell, although apparently uninjured, had been destroyed.

Substantia Nigra: Definite neuronal damage of varying degree was observed within the substantia nigra in approximately 31 per cent of the cases of bulbar poliomyelitis. In most of these cases not more than 10 per cent of the cells were involved. In only one case did the damage

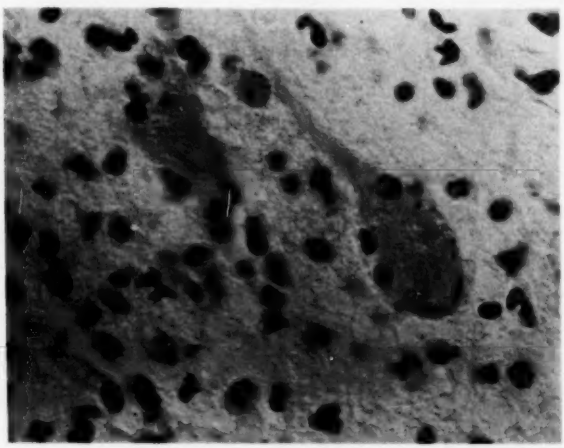


Fig. 6.—Two cells of the substantia nigra showing chromatolysis and neuronophagia. Only a finely granular pigment remains in the cell cytoplasm. Nissl stain.

involve as high as 75 per cent of the nerve cells. In most cases the pathological alteration consisted of a dissolution of the boxlike Nissl granules, neuronophagia, extrusion of the nucleus and fragmentation of the cell body (fig. 6). In a number of cells the end result of the destructive process consisted of a faint outline of the cell body filled with loosely arranged pigment. Macrophages filled with pigment material surrounded a number of these cells.

These cellular changes were usually focal in nature and were severest in the region of the most intense inflammatory reaction.

Oculomotor and Trochlear Nuclei: Because of the well documented normal histology of these cells, pathological alterations are readily detected (fig. 7). Although the fourth cranial nerve nucleus always

contained a mild inflammatory reaction, the neurons rarely showed any structural alterations. On the other hand, the cells of the third cranial nerve nucleus, although less consistently implicated in the inflammatory

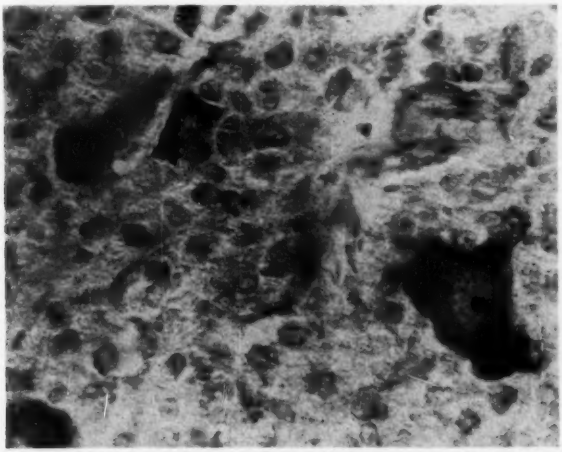


Fig. 7.—Nucleus of the oculomotor (third cranial) nerve from a patient with paralysis of the extraocular muscles. Note the chromatolysis and the fragmentation of the cells. Nissl stain.

Fig. 8.—Section through the lateral tegmental nucleus showing severe chromatolysis of the neurons with "ghost" cell formation. Nissl stain.

process, showed more frequent and more intense neuronal damage. In approximately 37 per cent of the cases of bulbar poliomyelitis neuronal damage appeared within the oculomotor nuclei. This damage frequently

implicated at least 50 per cent of cells. The inflammatory process within this nuclear group was generally mild, but became extremely intense in four cases and produced an inflammatory necrosis, resulting in destruction of all the neurons.

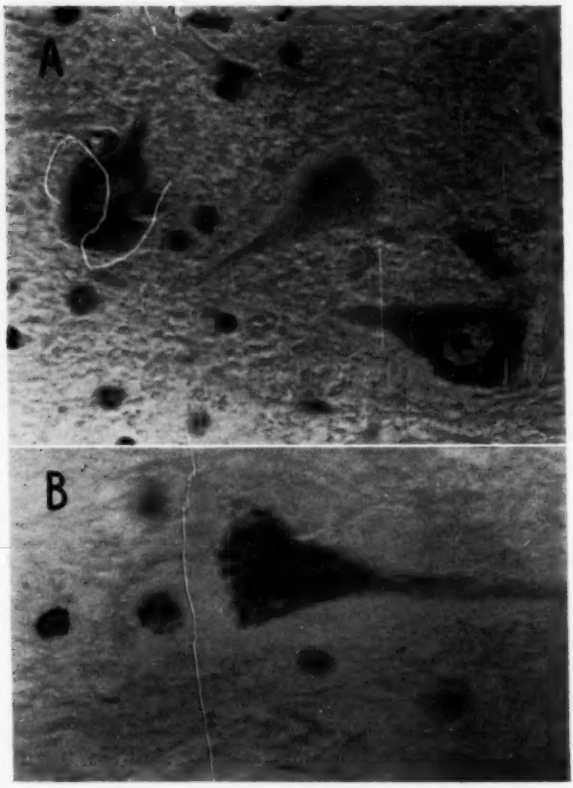


Fig. 9.—*A*, cells of the dorsal tegmental nucleus in a case of severe bulbar poliomyelitis. The cells are swollen and show almost complete chromatolysis. *B*, ventral tegmental nucleus, showing swelling and chromatolysis. Nissl stain.

Tegmental Nuclei: Cell alterations within the tegmental nuclei were more frequent than in any of the other structures of the midbrain. In general the lateral tegmental nuclei were more severely involved than the other two groups. In approximately 44 per cent of the cases neuronal changes were observed within this nuclear group, implicating from 2 to

50 per cent of the cells (fig. 8). The dorsal tegmental nucleus was damaged in about 22 per cent of the cases (fig. 9 *A*), and the ventral tegmental nucleus in 11 per cent (fig. 9 *B*). The involvement of these nuclear groups was usually milder than that seen in the lateral group but in the occasional case implicated at least 20 per cent of the cells. Rarely were the dorsal and ventral tegmental cells involved independently of the lateral tegmental cells, although the reverse was often true.

COMMENT

Although considerable information is available concerning the anatomic structure and the function of certain specific cell groups of the midbrain, such as the oculomotor nuclei and the substantia nigra, this does not hold true for the more numerous tegmental cells. These tegmental elements have been described, but little information is available concerning their specific cell structure, their function and their connections. Since the brain stem is severely involved in bulbar poliomyelitis, it was hoped that a study of the midbrain in this disease might elicit information concerning the function and the relation of these cells to other structures of the brain stem. Unfortunately, this has not been completely possible, primarily because of the acuteness of the illness in most of our patients. However, certain observations have been forthcoming which at least allow speculation as to the probable significance of these cell groups and their function. These conclusions can be drawn from various observations as regards structure and clinical-pathological correlation.

Structure.—From a structural point of view, the tegmental cells of the midbrain are definitely different from the reticular cells of the medulla. The tegmental cells are uniformly larger than those in the reticular formation. Invariably, the cytoplasm contains melanin. Some of the small cells of the lateral tegmental nucleus do bear a resemblance to the small reticular elements. However, these cells are few and constitute an exception to the general structure of the tegmental cells. The Nissl substance of the tegmental cells is uniform in structure and distribution, in contrast to the striking irregularity seen in the reticular cells. Therefore, if one assumes that the reticular cells have definite autonomic function, then, because of the structural difference of the tegmental elements, it would seem unlikely that the latter would have a similar function.

The question then arises as to the functions of these elements as judged from their structure. Certainly, the constant presence of melanin in these cells and their similarity, particularly those of the ventral tegmental nuclei, to the cells of the substantia nigra would lead one to favor the hypothesis of the participation of these cells in an extrapyramidal function, similar to that of the substantia nigra.

Clinical-Pathological Correlation.—Despite the fact that most of our patients died of acute bulbar symptoms, with severe clinical disturbance of the autonomic control of respiration and circulation, these symptoms did not correlate with the pathological changes observed in the tegmental nuclei. Similarly, there appeared to be no correlation between the severity of involvement of the tegmental nuclei and the involvement of the reticular cells of the medulla.

One might inquire as to the probable clinical function of these tegmental cells, particularly as to the apparent absence of symptoms associated with their destruction in our cases of bulbar poliomyelitis. We feel that the most logical explanation for the absence of apparent symptoms was the acuteness of the illness in most of the patients.

The same explanation may be offered for the apparent lack of specific symptoms in those cases with severe involvement of the substantia nigra. In approximately 6 per cent of our cases there was relatively intense damage to the substantia nigra, with at least 20 per cent of the cells injured or destroyed. One may assume that many more cells had been injured functionally. Still, in none of the cases were there any obvious symptoms of extrapyramidal damage. That extrapyramidal symptoms may occasionally occur in bulbar poliomyelitis may be accepted from the scattered cases of postpoliomyelitic parkinsonism reported in the literature (Marinesco and associates,[6] Vujic and Ristic [7] and Alajouanine and associates.[8]) In many other cases such symptoms might well result were it possible for all patients with bulbar poliomyelitis to survive. The high fatality rate in this disease no doubt is responsible for the small number of poliomyelitic patients who manifest a parkinsonian syndrome, assuming, of course, that involvement of the substantia nigra is responsible for this syndrome.

As to the function of the third nerve nucleus, little new information resulted from our studies. This nucleus was involved in 32 per cent of our cases. Because of the severity of their illness, many of the patients were not examined throughout the illness for involvement of the nuclei of the oculomotor (third cranial) nerve. For this reason, an accurate clinical-pathological correlation is difficult. It is apparent from our study, however, that whenever severe ocular symptoms were present extensive cellular damage was visible within the nuclei of the oculomotor nerve.

It has been assumed that in poliomyelitis the neuronal damage is the primary lesion and occurs independently of the inflammatory process. We have pointed out in previous studies [1] that, although the functional alteration depends on the damage to nerve cells, not uncommonly this cellular damage is entirely dependent on the more extensive inflammatory

process. This was particularly true of the changes within the midbrain. Whenever inflammatory changes were very widespread, the clinical course was fulminating, and death occurred within a few days.

CONCLUSIONS

1. The midbrain, although frequently involved in bulbar poliomyelitis, is never as severely implicated as the lower region of the brain stem.

2. Within the midbrain the severest involvement is generally observed within the oculomotor nuclei, the substantia nigra and the tegmental nuclei.

3. There are three sets of tegmental nuclei within the midbrain—the lateral, the ventral and the dorsal tegmental nuclei. Structurally, these cells do not resemble the reticular cells of the medulla but seem to be much more similar to the cells of the substantia nigra, to which they appear related.

4. Clinically, little evidence can be observed in patients with bulbar poliomyelitis to indicate extensive involvement of the tegmental nuclei.

5. In spite of the frequent and extensive involvement of the substantia nigra, little evidence of implication of the extrapyramidal system can be detected in cases of bulbar poliomyelitis. This is assumed to be due to the acuteness of the illness and the rapid fatality in these cases.

6. The oculomotor nuclei of the midbrain are only moderately implicated in bulbar poliomyelitis, and their involvement appears to correlate fairly well with ocular symptoms.

NEUROLOGICAL COMPLICATIONS OF RABIES VACCINE

Report of Two Cases

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J. E. WEBSTER, M.D.
AND
E. S. GURDJIAN, M.D.
DETROIT

WHEN Louis Pasteur[1] successfully prevented the appearance of rabies in Joseph Meister (1885) following the bite of a rabid dog, new hope was offered to persons who previously would have been condemned to certain death. However, in the years that followed it became apparent that the use of rabies vaccines was not without risk. Reports of various reactions, some fatal, began to accumulate in the literature, and the etiologic factors in these complications became a subject of dispute, which continues until the present day, some 64 years after the development of Pasteur's treatment.

The current literature reveals the difficulties in completely reporting each case of complications following antirabies therapy. Certain details are usually lacking; i. e., permission for necropsy may have been refused, the biting animal may not have been caught, the type of vaccine or the dosage may not have been known or an adequate history of the illness may not have been available. Therefore, when two cases of neuroparalytic accident associated with the prophylactic use of rabies vaccine U. S. P. occurred in Detroit within four months, we were prompted to report these cases as completely as was possible in the circumstances. Regrettably, certain particulars were lacking in these cases also.

REPORT OF CASES

CASE 1.—*History of earlier course of antirabies injections in childhood; development of transverse myelitis after 10 inoculations, with urinary retention, paralysis of lower extremities and sensory loss up to tenth thoracic dermatome; almost full recovery within 24 months.*

A 17 year old white youth, a student, was admitted to the Grace Hospital on Jan. 19, 1948, complaining of paralysis of both lower extremities. On Dec. 31, 1947 he had been bitten on the right cheek by a stray dog, which was not captured. First aid, consisting of local application of phenol after cleansing of the wound, was administered shortly after the bite. A course of antirabies treatment was advised, but the patient deferred reporting for the injections until January 5, when the first of daily injections of 1.5 cc. of rabies vaccine (Semple), prepared by the Michigan Department of Health, was given into the deltoid muscles. After the eighth consecutive daily injection, the patient began to complain of headache and stated that he felt "feverish." He received injections for the succeeding two days, and on January 16 urinary

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1. Vallery-Radot, R.: The Life of Louis Pasteur, translated by R. L. Devonshire, Garden City, N. Y., Garden City Publishing Company, Inc., 1926, pp. 414-417.

retention developed. Thereafter, he received no antirabies therapy. An indwelling catheter was inserted, and antibiotics were given. On January 18, "numbness and tingling" in both legs were noted, and the patient appeared somewhat lethargic. The next day the abdomen became distended, and he lost all voluntary control of his legs. With the onset of these symptoms, the patient was transferred to the Grace Hospital.

On admission to the hospital, the general physical examination revealed a well developed, well nourished, white youth, who appeared dehydrated and lethargic, with a blood pressure of 120/68, a pulse rate of 94 per minute, a respiration rate of 16 per minute and an oral temperature of 100.2 F. The heart, lungs and abdomen appeared normal. Neurological examination revealed inequality of the pupils, the right pupil being slightly larger than the left, and weakness of both upper extremities with hypoactive biceps and triceps reflexes bilaterally. There was complete, flaccid paralysis of both legs with absence of the patellar and achilles reflexes. Loss of pain and temperature sensations was apparent up to the tenth thoracic dermatome. A diagnosis of "acute postvaccinal encephalomyelitis" was made, and lumbar puncture revealed an initial pressure of 150 mm. of water, with a negative reaction to the Queckenstedt test. Web formation was noted in the fluid after 30 minutes.

The patient had received a previous series of antirabies injections at the age of 7 years. Allergy of any type in the immediate family or the personal history was denied.

Laboratory Data on Admission.—The results of a complete blood count were within normal limits; the urine contained a trace of albumin, a "few" white blood cells and 4 + red blood cells. The cerebrospinal fluid was "bloody" and contained 629 red blood cells and 1,181 leukocytes per cubic millimeter, of which 98 per cent were segmented granulocytes and 2 per cent were lymphocytes. The fluid showed a trace of globulin and a 1 + reaction for albumin and contained 58 mg. of sugar and 69 mg. of total protein, per 100 cc. The fluid was clear on centrifugation.

Hospital Course.—Penicillin and sulfadiazine therapy was instituted. The patient's neurological status remained unchanged for two days, and strength in the hands then began to improve, so that he could grasp objects firmly. By January 24 the deep reflexes in the upper extremities were active and perception of pain and light touch was acute down to the knees. The patellar reflex was absent, although the achilles reflex was present on both sides and there was a bilateral Babinski sign. The patient's temperature was normal and remained so during the rest of his hospital stay. On January 26 daily physical therapy, consisting of massage and passive motion of both lower extremities, was begun. Three days later the patient was able to move all toes of the right foot. At the time of his discharge from the hospital, on February 12, there was complete return of sensation throughout. Slight weakness of the lower extremities, with fecal incontinence, remained. Fluid obtained by lumbar puncture prior to discharge revealed 9 white blood cells per cubic millimeter, a negative reaction for globulin, a 1 plus reaction for albumin and a total protein of 60 mg. per 100 cc.

The patient was last seen on April 22, 1950. He was walking unaided, and his only complaint was that of urinary incontinence, particularly at night. His gait was normal, although the left lower extremity was slightly weaker than the right. There was no atrophy. The deep reflexes were all hyperactive, and an equivocal Babinski sign was observed bilaterally. There were no sensory deficits.

CASE 2.[2]—*History of previous antirabies vaccination in childhood; systemic reaction immediately after first antirabies inoculation, with development of encephalomyelitis and intercostal paralysis after eighth injection, terminating in death within 24 hours.*

A white man, aged about 25, a laborer, was bitten on the right ankle by a stray dog on Sept. 12, 1947. The animal was never apprehended. Pending capture of the animal, antirabies therapy was postponed until September 16, when further delay was thought inadvisable. Accordingly, on that date a course of rabies vaccine (Semple), from the Michigan State Department of Health, was begun, and daily injections of 1.5 cc. of the vaccine were given into the deltoid muscles. Almost immediately after the first injection, the patient complained of headache and "fever" and became nauseated. After each inoculation the reaction became worse,

2. Case 2 is presented through the courtesy of Dr. Joseph G. Molner, Commissioner, Department of Health, Detroit.

and at the time of the fifth injection the site of administration became indurated, red and painful. On September 20 the treatment was discontinued, and the symptoms disappeared for the ensuing two days. Treatment was resumed on September 23, 24 and 25, and the following day the patient had soreness in the back of the neck, numbness in the hands, feet and gums and several episodes of vomiting. On September 27, he began to "hurt all over," continued to vomit, with repeated hiccuping, and perspired profusely. The temperature at this time rose to 101 F. A lumbar puncture was done. The cerebrospinal fluid was found to contain 8 white blood cells per cubic millimeter and 81 mg. of sugar and 64.7 mg. of total protein, per 100 cc. On the morning of September 29 the patient was lethargic and had respiratory difficulty. He was hospitalized at 2:40 p. m., became comatose at 7:00 p. m. and died at 8:35.

On admission the patient appeared moribund and cyanotic. Respiration was labored and diaphragmatic in type, with complete paralysis of the intercostal muscles. There was no nuchal rigidity, and he responded but feebly to the spoken word. He was immediately placed in the respirator, and oxygen was given through a nasal catheter. Supportive measures, in the form of 1,000 cc. of 10 per cent dextrose in saline solution and frequent aspirations of the throat, were of no avail.

The past history of the patient revealed that he had been in the military service and had received all routine inoculations without sequelae. There was no history of allergic reactions of any type, but the patient had received more than 10 injections of rabies vaccine as a child. Hay fever was present in the patient's relatives.

Necropsy.—There were two recent linear scars on the right ankle above and below the external malleolus, reddish in color, the result of the animal bite. The lungs were darker than normal and were soggy, having the appearance of passive congestion. Reflection of the dura revealed diffuse, grayish thickening of the leptomeninges over the vertex. This was especially pronounced near the midline of both parietal lobes. Dissection of the meninges showed this process to be an increase in connective tissue, not exudative. The brain was soggy, and the blood vessels of the leptomeninges and cerebral parenchyma were moderately congested. The cortex and gray matter of the medulla appeared darker than normal. There was some convolutional flattening over the convexities of the hemispheres. Both sphenoid sinuses contained moderate amounts of thick, grayish yellow, mucopurulent material with reddening and thickening of the mucous membrane. A culture of this discharge produced "Pneumococcus type XIII, diphtheroid bacilli and hemolytic Staphylococcus pyogenes var. albus." The spinal cord below the upper cervical segments was not removed.

One-half the brain was submitted to the Bureau of Laboratories of the Michigan Department of Health for examination. Dr. G. D. Cummings, Director, reported that Negri bodies were not seen on direct examination. Test animals inoculated for rabies, poliomyelitis and encephalitis exhibited no evidence of illness during the trial periods.

The other half of the brain, the thoracic sympathetic trunks, major portions of the vagus nerve, lumbar plexuses and blocks from the psoas, rectus abdominis, pectoral and intercostal muscles were sent to the Brain Disease Registry of the Wayne University College of Medicine. The Detroit Department of Health received the following description of the pathological examination from Dr. Gabriel Steiner, neuropathologist.

Microscopic Study: There is widespread inflammation in the brain itself, the process being much less intense in the leptomeninges. The inflammatory response consists of adventitial infiltration with lymphocytes, plasma cells and a few segmented granulocytes (polymorphonuclear leukocytes) in thick cuffs. There is also a perivascular reaction in the surrounding parenchymal tissues, especially in the white matter. Here the cellular increase consists chiefly of microglial cells. The gray matter, except the cortex, may be somewhat more involved than the white matter. Prominent inflammatory lesions are seen in the hippocampus and around the aqueduct, the posterior horn and the floor of the fourth ventricle. An especially interesting observation is that of inflammatory lesions in peripheral nerves (vagus), which consist of diffuse infiltration with segmented granulocytes. The sympathetic ganglia and nerves show scanty lymphocytic infiltration. Negri bodies are not noted.

The diagnosis is encephalitis following the Pasteur treatment, with pronounced lymphocytic infiltration, and purulent diffuse endoneuritis of the vagus nerve.

GENERAL CONSIDERATIONS

Reactions to antirabies therapy have been completely described and classified by Horack.[3] His seven groups may be combined under two main heads: the extraneural and the neural type. Extraneural complications, which do not primarily involve the nervous system, are of two types:

1. The appearance in sensitized persons soon after the institution of treatment of a generalized urticarial rash, which responds to epinephrine.

2. Local reactions, with or without systemic involvement, varying from simple redness, swelling and induration at the site of injection to a severe local response, attended with headache, malaise, fever and lymphadenopathy. It is entirely possible that Joseph Meister had this type of reaction under Louis Pasteur's treatment, since Vallery-Radot [4] quotes Pasteur's observations on the child:

The last three inoculations have left some pink marks under the skin, gradually widening and not at all tender. There is some action, which is becoming more intense as we approach the final inoculation, which will take place on Thursday, July 16.

TABLE 1.—*Incidence of Neuroparalytic Complications Resulting from Use of Rabies Vaccine*

Location	Vaccine	Patients Treated	Reported Cases of Neuroparalytic Accidents
Alabama (Denison, G. A., and Dowling, J. D.: J. A. M. A. **113**: 390-395 [July 29] 1939)	Semple	33,147	1:8,287
Los Angeles County (Redewill, F. H., Jr., and Underwood, L. J.: California Med. **66**: 360-362 [June] 1947)	.....	2,389	1:1,194
North Carolina [3]	Calmette	24,000	1:1,200
Columbus, Ohio	Cord method	1,680	1:280
(Phillips, J. M.; Berry, F., and Snook, J. H.: J. Infect. Dis. **29**: 97-108 [July] 1921)	Dilution method	2,268	1:2,268
Georgia (Sellars, T. F.: J. M. A. Georgia **35**: 132-133 [April] 1946)	.....	50,000 (approximately)	1:7,142
Total		113,484	1:2,834

The neural type of reaction, affecting the nervous system, usually falls under one of three forms:

1. The peripheral form, commonly involving the facial nerve. Complete recovery is usual.

2. The spinal form, occurring after a preliminary severe local reaction and manifesting itself either as dorsolumbar myelitis, with paresthesias, sphincter disturbance and paralysis of the lower extremities, or as an ascending paralysis of the Landry type.

3. The cerebral form, without paralysis, characterized by a prodrome of adenopathy, malaise, headache and inflammation at the site of injection and the subsequent development of drowsiness, nuchal rigidity and signs of increased intracranial pressure, i. e., bradycardia and papilledema.

The incidence of neuroparalytic accidents complicating the use of rabies vaccine has been variously reported by American authors as ranging from 1:280 treated patients, in a small series, to 1:8,287 patients receiving the vaccine (table 1).

3. Horack, H. M.: Allergy as a Factor in the Development of Reactions to Antirabic Treatment, Am. J. M. Sc. **197**:672-682 (May) 1939.

4. Vallery-Radot,[1] p. 416.

On the other hand, worldwide statistics, reported by Greenwood,[5] place the incidence at 1:5,814 in a series of 1,290,758 treated patients, with a mortality of 25 per cent.

In 22 cases of neurological reactions to rabies vaccine collected from the literature[6] the large majority of the patients were between 20 and 40 years of age, and the males outnumbered the females by more than 2:1. The mortality in this group was 40 per cent.

In Michigan, approximately 6,000 patients received 84,122 doses of rabies vaccine from July 1, 1945 through March 31, 1949. During this period, 12 cases of reactions of all types to rabies vaccine, including four cases of neuroparalytic accident with one death, were reported to the Michigan Department of Health.[7] This represents 1 case of postvaccinal involvement of the nervous system for 1,500 patients treated (table 2).

Of the many theories concerning the etiology of reactions to antirabies treatment,[8] those with current support may be divided into two groups: those which implicate the nerve tissue in the vaccine as the causative agent and those which assume a culpable virus.

Proponents of the former hold that the reactions are due to the toxic effect of a constituent of nerve tissue in the inoculant on the nervous system of the recipient, or that they are anaphylactic or allergic responses to repeated injection of nerve proteins in the vaccine. It is the belief of Stuart and Krikorian [6o] that the accidents are due to the injected brain tissue, and they postulate the presence of a "cytotoxin" in normal brain tissue. To support their views, they offer experimental studies with animals in which paralyses were produced by the injection of both homologous

5. Greenwood, M.: Tenth Report on Data of Anti-Rabic Treatments Supplied by Pasteur Institutes, Bull. Health Organ., League of Nations **12**:301-364, 1945-1946.

6. (*a*) Horack.[8] (*b*) Ansell, I.: A Fatal Case of Myelitis After Antirabic Vaccine, Brit. M. J. **2**:338-340 (Aug. 14) 1948. (*c*) Bassoe, P., and Grinker, R.: Human Rabies and Rabies Vaccine Encephalomyelitis: A Clinicopathological Study, Arch. Neurol. & Psychiat. **23**:1138-1160 (June) 1930. (*d*) Breed, W. B.: Paralysis Following Antirabic Treatment with Case Report, New England J. Med. **202**:151-153 (Jan. 23) 1930. (*e*) Bussell, L. J.: Myelitis After Antirabic Vaccine: Report of Fatal Case, Lancet **2**:826-827 (Dec. 7) 1946. (*f*) Halle, S.: Post-Rabies Vaccine Paralysis, New Orleans M. & S. J. **101**:47-52 (Aug.) 1948. (*g*) Herron, P.: Fatal Paralysis Following Antirabic Treatment, ibid. **93**:446-450 (March) 1941. (*h*) Imrie, A.: A Case of Paraplegia Following Anti-Rabic Vaccination, J. Roy. Army M. Corps **83**:196-198 (Oct.) 1944. (*i*) Kiely, C. E.: Paralytic Accidents of Anti-Rabic Treatment, J. Med. **15**:68-78 (April) 1934. (*j*) Koenigsfeld, E.: Neuroparalytic Accident Following Anti-Rabic Vaccination, J. Roy. Army M. Corps. **85**:254-255 (Nov.) 1945. (*k*) Lindemulder, F. G.: Paralysis Following the Prophylactic Inoculation of Rabies Vaccine and Tetanus Antitoxin, J. Nerv. & Ment. Dis. **86**:284-291 (Sept.) 1937. (*l*) Murphy, W. B.: Paralysis Induced by Anti-Rabic Treatment, South. Med. & Surg. **94**:156-157 (March) 1932. (*m*) Pickar, D., and Kramer, H.: Encephalitis Complicating Vaccination for Rabies, South. M. J. **42**:127-129 (Feb.) 1949. (*n*) Smith, J., and Murphy, J.: Fatal Paralysis Following Antirabic Treatment, New England J. Med. **202**:153-154 (Jan. 23) 1930. (*o*) Stuart, G., and Krikorian, K. S.: Neuro-Paralytic Accidents of Antirabies Treatment, Ann. Trop. Med. **22**:327-377 (Nov.) 1928; (*p*) A Fatal Neuroparalytic Accident of Antirabies Treatment, Lancet **1**:1123-1125 (May 24) 1930; (*q*) Neuroparalytic Accidents Complicating Antirabic Treatment, Brit. M. J. **1**:501-504 (March 25) 1933. (*r*) Thomas, C. R.: Complications Following Use of Antirabic Vaccine with Suggestions as to Treatment, South M. J. **37**:539-543 (Oct.) 1944.

7. Cummings, G. D.: Personal communication to the authors.

8. Van Rooyen, C. E., and Rhodes, A. J.: Virus Diseases of Man, New York, Thos. Nelson & Sons, 1948, pp. 876-887.

TABLE 2.—*Data on Twelve Cases of Reactions to Rabies Vaccine in Michigan* *

Patient			Number of Injections Before Appearance of Symptoms	Vaccine Treatment After Appearance of Symptoms	Symptoms	Results
Sex	Age, Yr.	Vaccine Lot				
F	School age	...	11	Series discontinued	Encephalitis; some paralysis	Full recovery
M	About 25 (case 2)	535	1	Series discontinued for 2 days after 5th injection; total of 8 injections given	Headache, fever, nausea shortly after 1st injection; induration, pain and redness at inoculation site after 5th injection	Death within 24 hours of last dose
M	17 (case 1)	536	8	Series discontinued	Ascending paralysis	April 22, 1950: Normal gait; nocturnal incontinence of urine; hyperactive deep reflexes with equivocal Babinski sign bilaterally
F	10	...	4	Series resumed after 2 days; total of 10 injections given	Headache, vomiting, temperature of 102 F. after 4th dose; encephalitis and myelitis after 10th dose	Recovery, slight difficulty in walking still shown 20 days after release from hospital
M	..	546	4	Series discontinued	Violent cutaneous reaction	Recovery
M	43	†	9	Series discontinued	Headache; temperature of 102 F.; slight local reactions	Recovery
M	47	†	8	Series discontinued	Headache; temperature of 102 F.; slight local reaction	Recovery
M	50	†	6	Series discontinued	Chills; high temperature; malaise	Recovery
F	..	†	6	Series discontinued	Chills; high temperature; malaise	Recovery
F	38	†	11	Series discontinued	Chills; high temperature; pressure pains in head; stiff neck; dizziness	Recovery
M	43	†	13	Series discontinued	Headache; dizziness; vomiting; loss of coordination	Recovery
M	8	†	5	Series discontinued	Chills; high fever; stupor; malaise	Recovery

* These cases represent a period from July 1, 1945 to March 31, 1949.
† All reactions were reported within a month. This lot was withdrawn from distribution.

and heterologous normal brain substance. They concede, however, that an individual idiosyncrasy on the part of the patient may be important. On the other hand, Hurst [9] concludes from his investigations that the evidence is insufficient to prove that the injected brain tissue per se is responsible for the syndrome.

Schwentker and Rivers [10]; Kabat, Wolf and Bezer,[11] and Morrison [12] state that their laboratory researches have led them to believe that a serologic response, the production of antibodies against an antigen, takes place to the injection of emulsions of nerve tissue. Kirk and Ecker,[13] in transposing the work to human subjects, report that they found an increased antibrain antibody titer in the serum of a patient in whom encephalitis developed after antirabies therapy. These findings lend credence to the theory that reactions to rabies vaccines are anaphylactic or allergic. Horack [8] reports that the incidence of a personal or a familial history of allergy was significantly greater in a group of patients who exhibited reactions to rabies vaccine than in a control group who tolerated the injections without complication.

It cannot be denied that anaphylactic reactions to the prophylactic use of rabies vaccine do occur. Dorfman [14] describes one case in which a syncopal attack with a pseudopodial wheal and generalized urticaria appeared within a short time after the injection of Semple vaccine. Epinephrine was administered, and the symptoms disappeared. It was proved that the patient was hypersensitive to rabbit dander.

Pickar and Kramer [15] and Slipyan [16] report successful treatment of reactions to rabies vaccine with antihistamine drugs. Sellars [17] feels that the history of previous courses of antirabies therapy in five of seven of his cases with reactions to the vaccine is a "frequency which is beyond the realm of pure chance."

An interesting observation is the fact that prior to the development of better methods of epileptic control, injections of brain emulsions were given to epileptic patients to reduce the seizure rate. Stavrovskaya [18] reports the treatment of 60 epileptic patients with injections of 1 cc. of spinal cord emulsion which was allowed to stand 24 hours prior to use. He states that injection of the cord emulsion for as

9. Hurst, E. W.: The Effects of the Injection of Normal Brain Emulsion into Rabbits, with Special Reference to the Aetiology of the Paralytic Accidents of Antirabic Treatment, J. Hyg. **32**:33-44 (Jan.) 1932.

10. Schwentker, F. F., and Rivers, T. M.: The Antibody Response of Rabbits to Injections of Emulsions and Extracts of Homologous Brain, J. Exper. Med. **60**:559-574 (Nov.) 1934.

11. Kabat, E. A.; Wolf, A., and Bezer, A. A.: The Rapid Production of Acute Disseminated Encephalomyelitis in Rhesus Monkeys by Injection of Heterologous and Homologous Brain Tissue with Adjuvants, J. Exper. Med. **85**:117-130 (Jan. 1) 1947.

12. Morrison, L. R.: Disseminated Encephalomyelitis Experimentally Produced by Use of Homologous Antigen, Arch. Neurol. & Psychiat. **58**:319-416 (Oct.) 1947.

13. Kirk, R. C., and Ecker, E. E.: Time of Appearance of Antibodies to Brain in the Human Receiving Anti-Rabies Vaccine, Proc. Soc. Exper. Biol. & Med. **70**:734-737 (April) 1949.

14. Dorfman, W.: Hypersensitivity to Rabies Vaccine, New York State J. Med. **40**:215-216 (Feb. 1) 1940.

15. Pickar, D. N., and Kramer, H. M.: Encephalitis Complicating Vaccination for Rabies, South. M. J. **42**:127-129 (Feb.) 1949.

16. Slipyan, A.: Control of Allergy to Antirabic Vaccine, Ann. Allergy **6**:428-430 (July-Aug.) 1948.

17. Sellars, T. F.: Limitations of Antirabic Treatment, J. M. A. Georgia **35**:132-133 (April) 1946.

18. Stavrovskaya, M. N.: Treatment of Epilepsy with Brain Extract, Klin. med. **6**:1187-1196, 1928.

long as three years produced no undesirable complications. Kimball and Gudakunst [19] placed 106 patients with convulsive disorders under a regimen consisting of daily intramuscular injections of 2 cc. of a 10 per cent suspension of lipids from sheep brain. Five injections a week for six weeks comprised one course of treatment. An interval of one month was allowed to elapse, and the treatment was then resumed. In 10 per cent of the patients a slight local reaction developed at the site of inoculation and disappeared in two to three days, although none exhibited any severe reaction.

Admittedly, these series are small. It would seem reasonable, however, that if the complications of rabies vaccine therapy are due to the injected nerve tissue per se, these patients would be likely candidates for severe reactions, since they received far greater doses than the average person who is being treated after an animal bite.

Another group of investigators subscribe to the hypothesis that the reactions to the vaccine are caused by a virus. Bassoe and Grinker [6c] conclude that the fixed virus present in the inoculum is responsible. They base their deductions on similarities in the microscopic and gross pathology of rabies vaccine encephalomyelitis, true rabies and nonvaccinal encephalomyelitis complicating smallpox. While filtering phenolized vaccines through a wire sieve, Kelser [20] recovered some relatively coarse particles, which were suspended in saline solution and injected intracerebrally into rabbits. Fixed virus rabies was produced in these animals. It is his contention that phenolizing the vaccine "seared" the particles and protected the virus in the deeper portions. Therefore, he reasons, viable fixed virus can, and often does, become pathogenic.

Babonneix and Sigwald [21] postulate that the fixed virus in the vaccine activates a latent micro-organism present in the nervous system of the recipient of the vaccine. They draw a parallel between this action and that of the virus in smallpox vaccine, which, according to Levaditi and Nicolai, sensitizes the nervous system of the person inoculated to the virus of herpes encephalitis.

Marsden and Hurst [22] believe that measles, smallpox and antirabies vaccination are predisposing factors to an independent exanthem, which they term "acute perivascular myelinoclasis." As proof, they cite observed clinical and pathological resemblances in the so-called neurological complications of these diseases.

PATHOLOGY

Descriptions of pathological changes were found accompanying the recent reports of fatal neuroparalytic accidents.[23] There is almost complete agreement

19. Kimball, O. P., and Gudakunst, D. W.: A Study of Epilepsy in Detroit: A Preliminary Report, J. Michigan M. Soc. **35**:641-644 (Oct.) 1936.

20. Kelser, R. A.: The Epidemiology and Prophylaxis of Rabies, in Virus and Rickettsial Diseases with Especial Consideration of Their Public Health Significance, Cambridge, Mass., Harvard University Press, 1940, pp. 642-659.

21. Babonneix, L., and Sigwald, J.: Paraplégie flasque au cours du traitement antirabique, Ann. de méd. **26**:114-130 (July) 1929.

22. Marsden, J. P., and Hurst, E. W.: Acute Perivascular Myelinoclasis ("Acute Disseminated Encephalomyelitis") in Smallpox, Brain **55**:181-225 (June) 1932.

23. (*a*) Ansell.[6b] (*b*) Bassoe and Grinker.[6c] (*c*) Bussell.[6e] (*d*) Herron.[6g] (*e*) Smith and Murphy.[6n] (*f*) Getzowa, S.; Stuart, G., and Krikorian, K. S.: Pathological Changes Observed in Paralysis of the Landry Type: A Contribution to the Histology of Neuroparalytic Accidents Complicating Antirabic Treatment, J. Path. & Bact. **37**:483-500 (Nov.) 1933.

among the authors regarding the gross alterations of the nervous system. The changes, when present, were minor, consisting of injection of the vessels of the pia, brain or spinal cord, together with an occasional small hemorrhage. Herron,[6g] alone, describes a thin, cloudy exudate at the base of the brain.

Microscopically, the meninges were usually swollen, and occasionally round cell and erythrocyte infiltration was seen. Alterations in ganglion cells were observed in six of the seven cases. These changes varied from simple swelling and early nuclear changes to karyolysis and karyorrhexis. Bassoe and Grinker[6c] noted capillary abnormalities ranging from mild swelling of the endothelial cells to marked swelling with obliteration of the capillary lumens. They also observed pronounced proliferation of oligodendroglia in the cortex and cerebral white matter with areas of complete demyelination surrounding the blood vessels.

Perivascular "cuffing" with lymphocytes and erythrocytes was seen in three of the cases, but Getzowa, Stuart and Krikorian[23f] state that there were no infiltrations of the adventitial lymphatics; there was, however, enlargement of the perivascular spaces.

COMMENT

Several points in the foregoing presentation merit further comment. As may be seen from table 2, eight of 12 reported reactions of all types were to the same lot of vaccine, and all were observed within one month. All these complications were similar and were extraneural in type.

The explanation for this occurrence may lie in one of several factors. It may reflect the periodicity of appearance of an independent exanthem, as pointed out by Greenfield[24] and Marsden and Hurst.[22] This would seem unlikely, however, since in none of the cases did the condition progress to a typical encephalitic or myelitic syndrome.

On the other hand, it is conceivable that some constitutent of that lot of vaccine was responsible for the complications, since recovery followed discontinuation of the inoculation series in every case. As is the usual procedure, this vaccine had been tested for toxicity, viability, sterility, safety and potency in accordance with the requirements of the National Institute of Health. Nothing unusual was recorded from these laboratory assays.

Case 1 follows rather closely the established pattern of the spinal form of complications following use of rabies vaccine. The patient, after eight consecutive injections, noted headache and malaise. After the tenth inoculation he complained of urinary retention, and there subsequently developed a typical tranverse thoracic myelitis with no further antirabies prophylaxis. After a protracted convalescence, there was almost complete recovery. It should be reemphasized that this patient had received rabies vaccine on a previous occasion. This, in conjunction with a similar history in case 2, offers further substantiation of Halle's[6f] statement that grave danger accompanies a second course of antirabies inoculations.

Case 2 reveals details which warrant discussion. The patient's first injection was followed almost immediately by a severe systemic reaction. The rapidity of appearance would seem to indicate that this was the response of a previously sensitized person. The patient as a child had received a course of 10 injections of rabies

24. Greenfield, J. G.: The Pathology of Measles Encephalomyelitis, Brain **52**:171-195 (July) 1929.

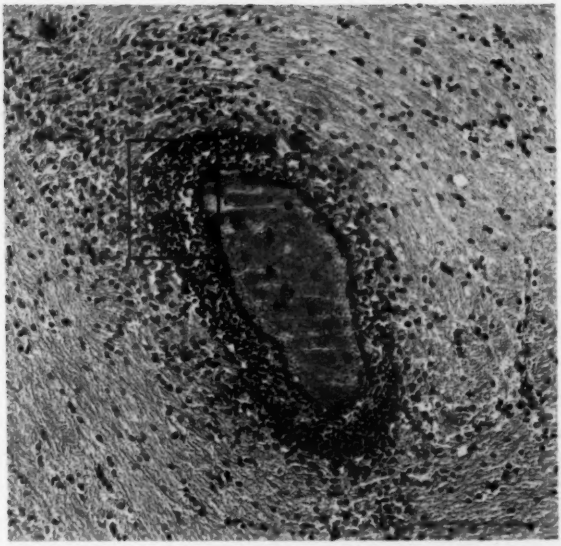

Fig. 1 (case 2).—Cerebral white matter, showing adventitial infiltration, with perivascular glial reaction in surrounding parenchyma. Hematoxylin and eosin stain; × 100.

Fig. 2 (case 2).—High power view (× 600) of the area indicated in figure 1. The infiltrative cells are lymphocytes, plasma cells and a few segmented granulocytes (polymorphonuclear leukocytes).

vaccine. Coupled with this fact is the temporary disappearance of the symptoms with interruption of the treatment course. If the reaction had been produced by a virus, as has been postulated, it does not appear reasonable that there should have been complete remission in the syndrome until the administration of the vaccine was again begun.

The disclosure at necropsy of a sphenoid sinusitis in case 2 must not be overlooked as a possible causative agent. Several findings, however, militate against the diagnosis of intracranial extension of sphenoid sinusitis. First, the spinal fluid contained only 8 cells per cubic millimeter, and the sugar level was 81 mg. per 100 cc. Second, there was complete absence of gross meningeal exudate, and

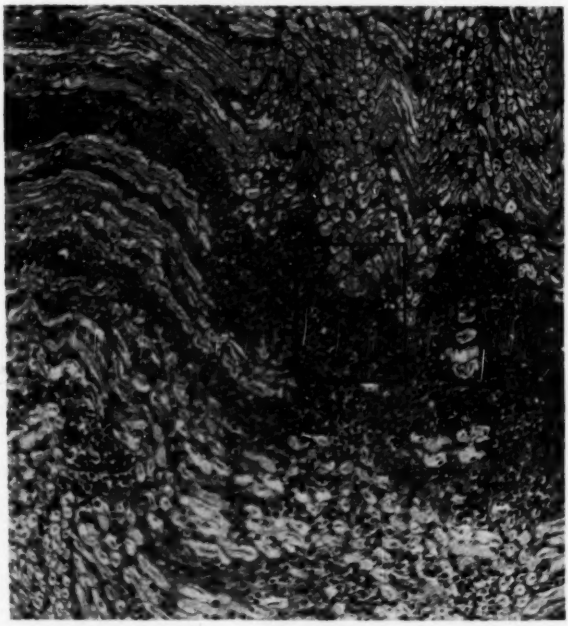

Fig. 3 (case 2).—Vagus nerve, showing diffuse infiltration with segmented granulocytes. Hematoxylin and eosin stain; × 100.

microscopically the leptomeningeal infiltrate was sparse and composed primarily of lymphocytes. The probability is that if the organisms cultured from the sphenoid sinus (Pneumococcus, type XIII, diphtheroid bacilli and hemolytic Staph. coccus pyogenes var. albus) were responsible for the disease in this patient, the gross and microscopic changes in the meninges would have been of the acute type and the alterations in the cerebrospinal fluid profound.

The pathological changes observed in case 2 are in accord, in general, with those described previously.[23] There were no prominent gross alterations of the nervous system. The microscopic changes were characterized by cerebral adventitial infiltration, or "cuffing," with round cells and a few segmented granulocytes (fig. 2).

Perivascular microglial reaction was in evidence throughout the brain and brain stem (fig. 1). Negri bodies were not found.

Of particular interest was infiltration of the vagus nerve with segmented granulocytes (figs. 3 and 4). Marinescu and Draganesco [25] describe lymphocytic infiltrations in certain peripheral nerves, i. e., the posterior tibial, in one of their cases, but apparently purulent endoneuritis in complications of antirabies vaccination has not previously been seen. Perhaps the vagus infiltration was in some manner attributable to the sphenoid sinusitis and was, therefore, peculiar to this case.

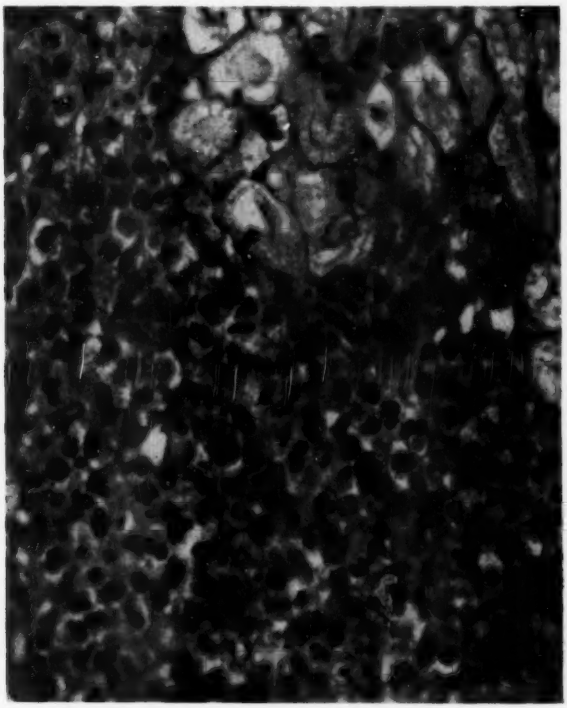

Fig. 4 (case 2).—Magnification of the field indicated in figure 3; × 600.

However, since the presence or absence of pathological changes in peripheral and cranial nerves was not recorded in the majority of reported cases of fatal reactions to the Pasteur treatment, it is difficult to evaluate the frequency of this finding. Consequently, an examination of the cranial and peripheral nerves would seem to be indicated in future cases.

25. Marinescu, G., and Draganesco, S.: Contribution à l'étude des accidents post-vaccino-rabiques (à l'occasion d'un cas avec examen anatomo-clinique), Ann. Inst. Pasteur **60**:477-498 (May) 1938.

SUMMARY

Two cases of neuroparalytic accident are reported. In both cases there was a history of previous antirabies treatment. In case 1 the condition was myelitic in type, with the appearance of thoracic transverse myelitis after the tenth inoculation and subsequent recovery. In case 2 it was encephalitic in character, with a systemic reaction following the first injection and the development of encephalomyelitis with intercostal paralysis after the eighth inoculation, the process terminating in death within 24 hours. Pathological changes included adventitial infiltration of cerebral vessels with round cells, perivascular microglial reaction and infiltration of the vagus nerve with segmented granulocytes (polymorphonuclear leukocytes).

The statistics of the Michigan Department of Health regarding complications of antirabies therapy for the period 1945 to 1949 are presented.

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The material in this paper from the Michigan Department of Health was made available to us by Dr. G. D. Cummings, Director, Bureau of Laboratories. Translation of the article by Stavrovskaya [18] was made by Dr. Peter G. Shifrin, Chief, Division of Orthopedics, Grace Hospital, Detroit.

CEREBRAL CIRCULATION IN POSTENCEPHALIC PARALYSIS AGITANS

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THE SYNDROME of paralysis agitans has been described as resulting from changes due to encephalitis, the so-called postinfectious form, and from vascular disease, the arteriosclerotic form. Vascular changes have been described in the pathology of acute and subacute epidemic encephalitis,[1] and in chronic cases calcification of vessels has been seen, such changes being associated with diseased nerve cells in the immediate environs. Indeed, some observers have remarked on the similarity of the pathological changes of the postencephalitic and arteriosclerotic forms of paralysis agitans.[2]

An occasional reference to the possible relation of these vascular changes to the causation of postencephalitic paralysis agitans has been made (Benda, in discussion on Alexander [3]), but attention in general has centered on the possibility of chronic infection or "delayed neurophysiological mechanisms" being the principal factor in its pathogenesis.[3] With the availability of a method for studying quantitatively the cerebral circulation of man,[4] we have attempted to evaluate the status of the cerebral circulation in a series of patients with postinfectious paralysis agitans.

METHOD AND MATERIAL

The cerebral blood flow of eight patients with postencephalitic paralysis agitans was determined by the nitrous oxide method.[4] The mean arterial blood pressure was obtained

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From the Neurosurgical and Neurological Services, Graduate Hospital of the University of Pennsylvania, and the Harrison Department of Surgical Research, University of Pennsylvania School of Medicine.

1. Wilson, S. A. K.: Neurology, edited by A. N. Bruce, Baltimore, Williams & Wilkins Company, 1940, pp. 133-136.

2. Wilson,[1] p. 801. Klaue, R.: Parkinsonsche Krankheit (Paralysis agitans) und postencephalitischer Parkinsonismus: Versuch einer klinischanatomischen Differentialdiagnose, Arch. f. Psychiat. **111**:251, 1940.

3. Alexander, L.: The Fundamental Types of Histopathological Changes Encountered in Cases of Athetosis and Paralysis Agitans, A. Research Nerv. & Ment. Dis., Proc. (1940) **21**:334, 1942.

4. Kety, S. S., and Schmidt, C. F.: The Nitrous Oxide Method for the Quantitative Determination of Cerebral Blood Flow in Man: Theory, Procedure and Normal Values, J. Clin Investigation **27**:476, 1948.

with a damped mercury manometer attached to a needle in the femoral artery. Blood gas analyses were made with the Van Slyke–Neill manometric apparatus. After quantitative measurement of the cerebral blood flow and determination of the oxygen contents of the arterial and internal jugular venous blood, the cerebral oxygen consumption ($CMRO_2$) was calculated from the transposed Fick formula:

$$CMRO_2 \text{ (u/100 Gm. brain/min.)} = CBF \times \frac{(A - V)}{100} O_2$$

where CBF is the cerebral blood flow.

The cerebrovascular resistance was calculated by dividing the mean arterial blood pressure by the cerebral blood flow.

Four of the eight patients, a few days after the initial cerebral circulatory studies, were subjected to bilateral resection of the stellate ganglion. A few days later, subsequent to their recovery from operation, quantitative observations on the cerebral circulation were repeated.

All eight patients gave a clear history of acute encephalitis. Six presented the usual picture of postencephalitic paralysis agitans, with rigidity and tremors and slow, steady progression of the disease process. Two of the eight patients studied (J. W. and M. K.) had marked abnormal movements, little rigidity, some euphoria, and excessive perspiration; although their symptoms appeared shortly after the initial infection and were indeed severe, there was little or no progression over a period of years.

RESULTS

For five of the eight patients (table) low values (averaging 28 per cent below normal) were obtained for the cerebral blood flow. One patient (C. V.) had a normal cerebral blood flow, and two (J. W. and M. K.) had greatly increased blood flows (26 per cent over normal). Interestingly, the latter two patients were the ones referred to as being more hyperkinetic and stationary in their symptoms. Likewise, the five patients with low cerebral blood flows had increased cerebrovascular resistance (63 per cent over normal); the three remaining subjects (C. V., J. W. and M. K.) had a normal cerebrovascular resistance. Seven of the eight patients had increased mean arterial blood pressures, averaging 23 per cent above normal. Four patients, all with reduced blood flows, had a striking reduction in cerebral oxygen consumption.

Considering the mean values for the entire series of eight patients, significant increases from normal average values were found in the mean arterial blood pressure ($p < 0.01$) and the cerebrovascular resistance ($p < 0.01$). The mean values for the cerebral blood flow and cerebral oxygen consumption were lower than normal in this entire series of patients, but the changes were not statistically significant. However, if the two patients clinically described as being hyperkinetic and having a stationary clinical course are eliminated, the mean values for the cerebral blood flow and oxygen consumption of the remaining six patients are also significantly reduced from normal.

Of the four patients subjected to bilateral stellate ganglionectomy, pronounced postoperative increases in the cerebral blood flow and decreases in the cerebrovascular resistance were noted in three (L. S., M. M. and W. N.). The latter three patients all had an initially decreased cerebral blood flow and increased cerebrovascular resistance, and these values returned to normal after operation. The remaining patient operated on (J. W.), who was hyperkinetic, had an initially rapid flow and normal or slightly decreased cerebrovascular resistance; both these functions were unaltered by operation.

Quantitative Data on Cerebral Circulation in Eight Patients Who Had Postinfectious Paralysis Agitans, with Effects of Bilateral Stellate Ganglionectomy in Four

Patient	Age	Sex	Internal Jugular Venous								Arterial								Cerebral Functions †									
			O_2 Content (Vol. %)		CO_2 Content (Vol. %)		p_H		CO_2 Tension, Mm. Hg		O_2 Content (Vol. %)		CO_2 Content (Vol. %)		p_H		CO_2 Tension, Mm. Hg		A-VO_2 (Vol. %)		R. Q.		C. B. F., Cc./ 100 Gm./ Min.		C. M. R., Cc./ 100 Gm./ Min.		C. V. R., Mm. Hg, Cc./ 100 Gm./ Min.		M. A. B. P. Mm./Hg	
			I *	II *	I	II	I	II	I	II	I	II	I	II	I	II	I	II	I	II	I	II	I	II	I	II	I	II	I	II
L. S.	38	M	11.8	10.8	53.5	55.4	7.33	7.38	48	44	17.3	15.4	48.4	51.7	7.38	7.41	41	41	5.5	4.6	0.93	0.80	37	50	2.0	2.3	3.2	1.9	119	95
M. M.	51	F	9.0	8.2	55.0	61.3	7.29	7.35	53	51	14.3	12.4	49.9	57.2	7.34	7.40	45	45	5.3	4.2	0.96	0.98	37	69	2.0	2.9	2.7	1.6	100	109
J. W.	27	M	12.8	12.1	52.8	55.3	7.35	7.35	46	47	18.2	15.9	48.3	51.8	7.41	7.39	38	42	5.4	3.8	0.83	0.92	71	68	3.8	2.6	1.4	1.4	99	96
W. N.	42	M	13.0	10.3	54.5	58.7	....	....	..	..	17.7	15.9	50.3	53.2	....	....	..	..	4.7	5.6	0.90	0.98	39	54	1.8	3.0	2.2	1.6	87	88
M. K.	35	F	12.0	....	46.0	....	....	....	..	..	17.6	....	40.2	....	....	....	..	..	5.6	...	1.03	....	65	..	3.6	...	1.6	...	107	..
W. H.	53	M	9.8	....	55.4	....	....	....	..	..	18.9	....	46.8	....	....	....	..	..	9.1	...	0.95	....	38	..	3.5	...	2.7	...	102	..
D. K.	28	M	12.6	....	48.9	....	....	....	..	..	17.3	....	43.9	....	....	....	..	..	4.7	...	1.06	....	45	..	2.1	...	2.1	...	96	..
C. V.	39	F	9.2	....	51.4	....	....	....	..	..	14.9	....	46.3	....	....	....	..	..	5.7	...	0.90	....	56	..	3.2	...	1.7	...	97	..
Mean	39	..	11.3	10.4	52.2	57.7	7.32	7.36	49	47	17.0	14.6	46.8	53.5	7.38	7.40	41	43	5.8	4.6	0.95	0.92	48.5	60	2.8	2.7	2.2‡	1.6	101‡	97
Normal Mean	..	..	11.0	....	55.0	....	7.37	....	50	..	18.0	....	50.0	....	7.42	....	40	..	6.3	...	0.99	....	54	..	3.3	...	1.6	...	86	..

* I indicates initial values; II, values after bilateral stellate ganglionectomy.
† C. B. F. denotes cerebral blood flow; C. M. R., cerebral metabolic rate (oxygen consumption); C. V. R., cerebrovascular resistance; M. A. B. P., mean arterial blood pressure.
‡ Significant variation from normal mean value.

COMMENT

Since the nitrous oxide method measures the over-all blood flow through the brain, any local changes in the brain, unless very extensive, would not be detected with this technic. Therefore, the decrease in circulation noted in five of the eight cases in this study may be presumed to reflect a general involvement of the cerebral vasculature and may thus be analogous to the general cerebral vascular changes of arteriosclerosis.[5] The pathogenesis of the progressive features of postinfectious paralysis agitans thus may not differ from that of paralysis agitans ascribed to primary vascular disease of the brain. This similarity of pathogenesis is further suggested by the resemblance of many histological features of these two forms of paralysis agitans.[2a]

The decrease in cerebral circulation appears, from the data, to be due to increased cerebrovascular resistance. Indeed, the increase in systemic blood pressure noted may well be a homeostatic effort to maintain the cerebral blood flow in the face of increased vascular resistance. The effects of bilateral stellectomy in all three patients operated on from this group of five with decreased cerebral blood flow identifies the existence of a large vasospastic element in the increased cerebrovascular resistance of these patients that is probably maintained by means of a sympathetic reflex mechanism. Organic vascular changes have been suggested to result from persistent vasospasm.[6] If this is so, it is conceivable that progressive parenchymal changes could occur in these patients with cerebral vasospasm and thus account for the progressive nature of their disease.

In the two patients clinically distinguished from the others as being hyperkinetic and having a stationary clinical course, the cerebral blood flow was above normal and the cerebrovascular resistance normal or below. In one of these patients bilateral stellate ganglionectomy did not alter the values found prior to operation. This further demonstrates that the absence of the vasospastic element may well be correlated with the lack of progression of the disease process in these two patients and emphasizes the probable significance of its presence in the remaining patients of the series studied, who clearly had a progressively deteriorating course.

In the four patients on whom bilateral stellate ganglionectomy was performed, despite the beneficial effects on the cerebral circulation noted in three, no clinical improvement occurred. It is difficult to believe that damage to centers sufficient to produce clinical changes of such long standing would be reversible. This does not preclude, however, the prevention of further damage to the brain and a favorable effect on the course of the disease.

SUMMARY

1. The cerebral circulation was studied quantitatively in a series of eight patients with postinfectious paralysis agitans.

2. Six patients of this series had a progressively deteriorating clinical course, and in this group a significant lowering of the cerebral blood flow and cerebral oxygen consumption and an increase in the cerebral vascular resistance were found.

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3. Two patients were noted to have stationary clinical courses; in addition, they manifested marked abnormal movements but little rigidity. The cerebral blood flow of both these patients was distinctly greater than normal, and the cerebrovascular resistance was normal or slightly decreased.

4. Bilateral stellate ganglionectomy in three patients with slowed cerebral blood flow and increased cerebrovascular resistance produced a change to normal in both functions.

5. Bilateral stellate ganglionectomy had no effect on the cerebral circulation of the one patient who had an initially rapid cerebral blood flow.

CONCLUSIONS

1. Alterations of the cerebral circulation may play a prominent role in the pathogenesis of postinfectious paralysis agitans.

2. In patients with postinfectious paralysis agitans and having a slowed cerebral blood flow due to increased cerebrovascular resistance, vasospasm played a major role in the increased cerebrovascular resistance, and this was relieved by bilateral stellate ganglionectomy.

MOTIVATIONS IN THE REHABILITATION OF PARAPLEGICS

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MANY medical specialists [1] believe that the rehabilitation of paraplegic patients needs to be supplemented with vocational counseling and training for work as soon as possible. Early vocational training has been found to facilitate rehabilitation.[2]

It is generally believed that the higher the level of the spinal cord injury, the greater will be the bodily involvement, usually resulting in the necessity of reeducation of physical activities. Several questions arise: From the point of view of vocational rehabilitation, would the level of the spinal cord injury affect the degree of motivation toward vocational or educational planning? Should one expect to find a larger percentage of paraplegic veterans seeking and developing training programs among those with lesions of the lower part of the cord than among those with lesions of the upper part? Once the paraplegic has selected specific employment objectives, would the level of injury influence his effort toward reaching his vocational goal? Questions of this type are frequently raised by persons working with paraplegic patients. The data presented in this paper may provide tentative answers to these questions.

PRESENT INVESTIGATION

Material.—During a period of three years—1946 through 1948—216 male paraplegic veterans were counseled by the Vocational Rehabilitation and Education section of the Veterans Administration Hospital, Van Nuys, Calif. (now moved to Long Beach, Calif.). Of these, 115 developed training programs leading toward specific employment objectives, while 101 did not complete their vocational advisements.

The group of 115 paraplegic veterans completing advisement had an age range of 18 to 53 years, with a mean age of 25.8 years. Eighty-nine per cent were white veterans; the rest included Mexican, Negro, Indian, Japanese and Filipino veterans. Sixty per cent were single; 35 per cent, married, and 5 per cent, divorced or separated. The educational range was from six to 16 years of schooling, with a mean of 11.1 years of schooling completed. Fifty-five per cent had been privates; 28 per cent noncommissioned officers, and 17 per cent, officers. Eighty-eight per cent were receiving compensation for service-connected disabilities and were eligible for rehabilitation benefits under Public Law 16; 12 per cent had non-service-connected disability and were eligible for educational benefits under Public Law 346.

Sponsored by the Veterans Administration and published with the approval of the Chief Medical Director. The statements and conclusions published by the author are a result of his own study and does not necessarily reflect the opinion or policy of the Veterans Administration.

1. (*a*) Bors, E.: Spinal Cord Injuries, Technical Bulletin TB 10-503, Washington, D. C., Veterans Administration, Dec. 15, 1948. (*b*) Thom, D. A.; Von Salzen, C. F., and Fromme, A.: Symposium on Problems in Postwar Medicine: Psychological Aspects of the Paraplegic Patient, M. Clin. North America **30**:473-480 (March) 1946.

2. Bors.[1a] Manson, M. P.: The Concept of Rehabilitation Applied to Paraplegia, Arch. Indust. Hyg. **1**:65-72 (Jan.) 1950. Thom and others.[1b]

The group of 101 paraplegic veterans not completing advisement had an age range of 20 to 51 years, with a mean age of 27.1 years. Ninety-two per cent were white veterans, while 4 per cent were Mexican and 4 per cent were Negro veterans. Fifty-eight per cent were single; 35 per cent were married, and 7 per cent were divorced. The educational range was from 3 to 15 years of schooling, with a mean of 10.2 years of schooling completed. Thirty-six per cent had been privates; 57 per cent, noncommissioned officers, and 7 per cent, officers. Seventy-six per cent had service-connected disability, and 24 per cent had non-service-connected disability.

Several statistically significant differences appeared between the two groups: The paraplegic group completing vocational advisement were younger, had completed more years of schooling and contained larger percentages of privates and officers but a smaller percentage of noncommissioned officers. It appears, therefore, that the younger and better educated paraplegics are more likely to form training programs than are the older and less educated paraplegics.

Of the total group of 216 paraplegic veterans, 84 per cent had been in the Army, 8 per cent in the Navy and 8 per cent in the Marine Corps.

Bors [3] noted that the distribution of spinal cord injuries by levels differs when wartime and peacetime paraplegic groups are compared, there being a considerably larger percentage of cervical lesions in peacetime paraplegic patients. The difference in percentages of cervical lesions between the wartime and the peacetime paraplegic groups is significant at the 1 per cent level of confidence. Such a difference is probably due to the greater number of diving and falling accidents in civilian life, leading to injuries in the region of the neck.

TABLE 1.—*Levels of Injury for Wartime and Peacetime Paraplegics*

Level	Wartime, % (N = 263) *	Peacetime, % (N = 76) *	Percentage of Cord Exposed	Combined Percentage (N = 339) *	Critical Ratio
Cervical	9	26	35	13	3.2
Thoracic	70	59	62	68	1.7
Below Th 12	21	15	3	19	1.3

* Data from Bors.[3]

It might be assumed that the percentages of wartime injuries according to spinal cord levels would depend on the amount of the spine exposed to damage. However, comparison of the percentages of exposed spine by levels with the percentages of injury shows but a slight relation between the two. Perhaps it is that on the battlefield injuries at higher levels carry higher mortality rates than do injuries at lower levels. Such an assumption might explain the smaller percentages of higher lesions and the larger percentages of lower lesions found by Bors [3] (table 1).

Method.—Statistical comparisons were made between the paraplegic group completing vocational advisement and the paraplegic group not completing vocational advisement according to levels of injury. The group completing vocational advisement was then followed through its training activities; and of this group, those active in training were compared with those inactive in training according to levels of injury.

Results.—When the group of paraplegic veterans completing vocational advisement was compared with the group not completing vocational advisement, no significant differences were found. Apparently, relatively equal percentages of patients for each level of injury will complete vocational advisement. It thus appears that motivation for the planning of a training program is not affected by the level of injury (table 2).

Paraplegic veterans completing vocational advisement nearly always developed plans which called for going to school or obtaining on-the-job training. The paraplegic veterans completing vocational advisement were divided into two groups:

3. Bors,[1a] p. 18.

(*a*) those actively engaged in their programs and (*b*) those inactive in vocational training.

No statistically significant difference between the active and the inactive group based on levels of injury were found (table 3). However, when the data in this table were further treated, a definite trend appeared which indicated that the percentages of paraplegics with lesions of the lower part of the cord who were vocationally active was slightly larger than that of paraplegics with lesions of the higher levels of the cord (table 4). Since the paraplegics with lesions of the lower part of

TABLE 2.—*Percentages Within Levels of Spinal Cord Injury of Paraplegic Veterans Completing and Not Completing Vocational Advisement*

Level	Completed, % (N = 68)	Not Completed, % (N = 61)	Combined Percentage (N = 129)	Critical Ratio
Cervical	10.3	14.8	12.4	0.8
Thoracic	66.2	57.4	62.0	1.0
Lumbar	22.1	21.3	21.7	0.1
Cauda equina	1.4	6.5	3.9	1.4

TABLE 3.—*Levels of Spinal Cord Injury of Paraplegic Veterans Relative to Vocational Activity or Inactivity*

Level	Active, % (N = 35)	Inactive, % (N = 33)	Combined, % (N = 68)	Critical Ratio
Cervical	8.6	12.1	10.3	0.5
Thoracic	65.7	68.7	66.2	0.1
Lumbar	22.8	21.2	22.1	0.2
Cauda equina	2.9	0	1.4	1.0

TABLE 4.—*Vocational Activity or Inactivity Within Levels of Injury*

	Active (N = 35)		Inactive (N = 33)		Combined Groups (N = 68)	
Level	No.	%	No.	%	No.	%
Cervical	3	42.9	4	57.1	7	100.0
Thoracic	23	51.1	22	48.9	45	100.0
Lumbar	8	53.3	7	46.7	15	100.0
Cauda equina	1	100.0	0	0	1	100.0

the cord had full use of the arms and hands, while many of those with injuries of the higher levels had involvement of the arms and hands, it would seem that vocational activity would depend, to a great extent, on the use of the arms and hands.

When the group completing advisement with school plans was examined with relation to activity or inactivity according to the level of injury, a trend appeared which indicated that those with injuries at the lower levels were more active than those with injuries at the higher levels (tables 5 and 6). Even in school activities, the arms and hands play a vital role.

Fewer paraplegics were interested in on-the-job training programs than in school training. Veterans with injuries at high levels showed smaller percentages of activity than did those with injuries at low levels. Although such a trend was present, it was not statistically significant (tables 7 and 8).

Of the paraplegics selecting objectives calling for school training, the chances were 2.7 : 1 that such programs would be activated; but for those selecting on-the-job training programs, the odds were 7.3 : 1 that such programs would not be activated. It seems clear, at this time, that school training programs are most feasible for the rehabilitation of paraplegic patients. School programs offer fewer

TABLE 5.—*Levels of Spinal Cord Injury Relative to School Activity or Inactivity*

Level	Active, % (N = 32)	Inactive, % (N = 11)	Combined, % (N = 43)	Critical Ratio
Cervical	9.4	9.1	9.3	0
Thoracic	65.6	81.8	69.8	1.3
Lumbar	21.9	9.1	18.6	1.3
Cauda equina	3.1	0	2.3	1.0

TABLE 6.—*School Activity or Inactivity Within Levels of Injury*

	Active (N = 32)		Inactive (N = 11)		Combined Groups (N = 43)	
Level	No.	%	No.	%	No.	%
Cervical	3	75.0	1	25.0	4	100.0
Thoracic	21	70.0	9	30.0	30	100.0
Lumbar	7	87.5	1	12.5	8	100.0
Cauda equina	1	100.0	0	0	1	100.0

TABLE 7.—*Levels of Spinal Cord Injury Relative to On-the-Job Activity or Inactivity*

Level	Active, % (N = 3)	Inactive, % (N = 22)	Combined, % (N = 25)	Critical Ratio
Cervical	0	13.6	12.0	1.9
Thoracic	66.7	59.1	60.0	0.5
Lumbar	33.3	27.3	28.0	0.4
Cauda equina	0	0	0	0

TABLE 8.—*On-the-Job Activity or Inactivity Within Levels of Injury*

	Active (N = 3)		Inactive (N = 22)		Combined Groups (N = 25)	
Level	No.	%	No.	%	No.	%
Cervical	0	0	3	100.0	3	100.0
Thoracic	2	13.3	13	86.7	15	100.0
Lumbar	1	14.3	6	85.7	7	100.0
Cauda equina	0	0	0	0	0	0

physical barriers to the paraplegic patient. Once, again, it appears that the use of arms and hands is of the greatest importance in motivating the paraplegic patient. Should adequate on-the-job training facilities become available to paraplegics, it is believed that increasing numbers of such patients would prefer such training; many paraplegics enter schools only because they realize the extreme difficulty that exists in obtaining on-the-job training.

A study by Weiss, reviewed by Bors,[18] of posthospital activities of paraplegic patients indicated that the lower the level of spinal cord injury, the greater the

probability that the paraplegic would find employment. Weiss also noted that paraplegics with injuries at higher levels tended to have larger percentages in schools than did those with injuries at lower levels. It is quite likely that paraplegics with injuries at lower levels, having more opportunities to accept work, leave schools to accept such work earlier than those with injuries at higher levels (table 9).

TABLE 9.—*Level of Injury in Relation to Employment, School Attendance and Nonremunerative Hobbies**

	Employment (N = 29)		School (N = 57)		Nonremunerative Hobbies (N = 35)		Total (N = 121)	
Level	No.	%	No.	%	No.	%	No.	%
Cervical	1	12.5	5	62.5	2	25.0	8	100.0
Upper thoracic	4	14.3	15	53.6	9	32.1	28	100.0
Lower thoracic	14	24.6	30	52.6	13	22.8	57	100.0
Lumbosacral	10	35.7	7	25.0	11	39.3	28	100.0

* From Bors [18]; data by Weiss.

SUMMARY AND CONCLUSIONS

Regardless of the level of spinal cord injury in paraplegic patients, motivation exists or can be created to the extent to which they will adopt training programs leading to specific employment objectives.

There is some evidence that the level of spinal cord injury will influence both school and on-the-job training activities. Paraplegics with injuries of the lower part of the cord had larger percentages engaged in active programs than did paraplegics with injuries of the higher part of the cord. It is believed that the greater the use of the arms and hands, the better will be the prognosis for an active rehabilitation program beyond the planning stage.

Probably, to a great extent because of inadequate on-the-job training facilities, many more paraplegic veterans select educational programs than on-the-job training programs. Paraplegics developing school programs had odds of almost 3:1 in their favor that they would start such programs, while those with on-the-job programs had odds of better than 7:1 against them that they would start such programs.

TESTING VISUAL FIELDS BY FLICKER FUSION

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ST. LOUIS

THE CRITICAL rate at which a flickering light of decreasing frequency is first perceived to flicker is the one test of visual function in which the light-adapted eye is more sensitive at the periphery of the retina than at its center. Previous investigators have agreed that flicker fusion fields are sensitive and "typical" in neurological lesions. Phillips [1] (1933) reported two cases of pituitary tumor in which flicker fusion fields proved superior to standard fields. He used a mechanical sector disk method, testing flicker fusion frequency in 17 areas of each field. Riddell [2] (1936) using a similar device and procedure, reported one case in which standard fields showed only a small temporal slant, while flicker fusion fields showed complete hemianopsia. Werner [3] (1942) found pronounced lowering of flicker fusion frequency in 41 patients with various disorders of the central nervous system. Hylkema [4] (1942) found that flicker fusion frequency decreased more in pathological conditions of the brain than in local retinal disease. He reported several cases of tumor in the occipital lobe and brain stem. He used the mechanical sector disk and measured 21 areas in each field. Enzer, Simonson and Blankstein [5] (1944) reported that 15 of 33 patients with definite lesions of the brain showed reduction of flicker fusion frequency of from one to nine flashes per second. Teuber and Bender [6] (1948) studied 28 war casualties with occipital wounds. All showed lowered flicker fusion frequency. Miles [7] (1949) found defective flicker fusion fields in 24 eyes in which early glaucoma could be demonstrated but standard fields were normal. The present paper reports 47 neurological cases.

From the Department of Ophthalmology and the Oscar Johnson Institute of the Washington University School of Medicine.

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METHOD

Whereas standard methods of taking fields test the perception of light, contrast, color and form on various parts of the retina, the flicker fusion technic tests merely the critical rate of fusion. Instead of the standard 330 mm. perimeter, the perimeter used (fig. 1) is 1,000 mm. from the eye being tested. This makes the projection of the blindspot great enough that the large flickering target can be placed accurately on several parts of its perimeter. Instead of the standard arc of more than 90 degrees from the fixation line, only a 30 degree arc is used. This conforms to the size of field commonly tested by the tangent screen used routinely by ophthalmologists. This standard gray felt surface marked off in three 10 degree

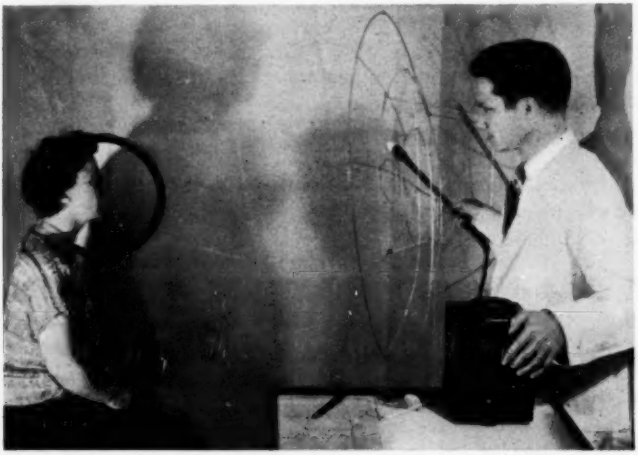

Fig. 1.—Use of the strobotac® for taking flicker fusion fields on the 1,000 mm. perimeter.

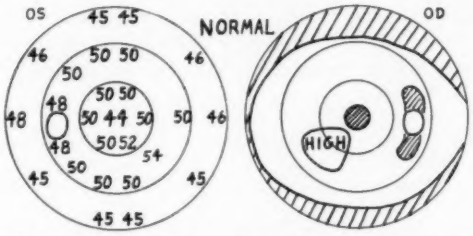

Fig. 2.—Normal flicker fusion field. The numbers refer to flashes per second, or flicker fusion frequency. Note that the central 3 degree area is low and that the highest flicker fusion frequency is inferior and nasal.

circles can be used with nearly equal precision in testing flicker fusion fields. Flicker fusion can be tested out to 90 degrees and beyond, but usually this extension of the test gives no additional information.

The blindspot lies between the 10 and the 20 degree ring and in the illustrations serves to designate the right and left eyes. Only in figure 2 are the eyes labeled *O.S.* and *O.D.* The test is carried out under ordinary room illumination, to which the patient has been adapted. The two eyes are tested separately without complete occlusion of the eye not being tested. Spectacles are used which occlude one eye only, with a white disk excluding only the target area.

The flickering light bulb used as a target is mounted at the end of a 6 foot (180 cm.) cable on a 2 foot (60 cm.) wand, so that it can be placed in any part of the visual field to be tested. The light is diffuse, yellow red and circular, with a diameter of from 3 to 4 cm. The light can be made yellow or white and should flicker with equal light and dark intervals at rates between 10 and 60 flashes per second. The diameter of the light must be large, because the flicker frequency falls to a clinically useless rate at the periphery when the diameter is less than 2 degrees of arc.

The present work was done with a constant flash duration of 10 microseconds. This makes the dark interval too long, and apparently in flicker fusion tests the "off-impulse" is just as important as the "on-impulse." The target bulb was driven by the strobotac® instrument,[8] which proved convenient and very dependable. The flicker frequency at any moment could be read with high precision on a dial in terms of flashes per second. Repeatability of this test is so high that the instrument cannot be too accurate.

The test is begun with a rate above flicker fusion, so that the target light appears steady. The rate is gradually reduced until the light definitely begins to flicker, when the patient reports "Now." One or two trial runs with fixation directly on the light suffice, as the patient comprehends this test easily. Flicker fusion frequency is taken in a routine order in 27 or more positions (fig. 2). If any area tested seems abnormal, it is given a few moments' rest while other areas are tested, but is always rechecked. Figure 2, *O.D.*, shows that the part of the field with the highest flicker rate is eccentric and that the lowest areas include the central 3 degrees and the areas just above and below the blindspot.

In field tests for neurological lesions, the comparison of "paired areas" across the vertical meridian is particularly important. This is for detection of quadrantoptic or hemianoptic field defects and is well illustrated in the case reports which follow.

These case studies were made in most instances by the neurological department of Washington University. The standard visual fields were taken by members of the resident staff of the department of ophthalmology.

CASE STUDIES

In the accompanying table are summarized data on 47 cases in which flicker fusion fields were compared with standard fields. The latter were taken for 3/330 white on the perimeter and for 1/1000 white on the tangent screen. Perhaps more revealing fields could have been obtained by using reduced illumination, a 2 meter distance and colored targets, but the expenditure of time and the discomfort to the sick patient make standard methods unpopular.

Figure 3 illustrates the fields of C. B., aged 24, which are typical of the nine cases of chiasmal tumor studied. He had an adenoma attached to the right optic nerve sheath which caused decrease of visual acuity to 6/100 in the right eye and 6/18 in the left eye, making preoperative standard fields useless. Flicker fusion fields (fig. 3*A*) showed almost complete temporal hemianopsia on the left and superior temporal quadrantopsia on the right. Postoperative flicker fusion fields showed general depression, particularly in the right eye, a temporal slant on the left and right hemianopsia. Standard fields (fig. 3*C*) correlated well. Repeated fields six months later showed the flicker fusion frequencies in the left eye and in the nasal half of the field of the right eye to be higher than normal (fig. 2), while standard fields showed no change in the right hemianopsia.

The five cases of parietal lesions showed a uniform absence of changes in the standard fields and a surprising presence of homonymous hemianopsia in the flicker fusion field, which always conformed to the side of the diseased hemisphere.

Similarly, in six of the nine cases of vascular diseases there were no changes in the standard fields. In five of the nine cases, flicker fusion fields revealed definite homonymous hemianopsia, conforming to the diseased side; in three they were less definite, and in only 1 did they show none.

8. Made for the past 15 years by General Radio Co., Cambridge, Mass.

Comparison of Flicker Fusion Fields and Standard Fields in Forty-Seven Cases of Neurological Lesions

A. Relation to Disease Type

Disease Type	Focus Localized					
	Standard Fields			Flicker Fusion Fields		
	None	Slightly	Well	Poorly	Well	Very Well
Chiasmal tumors (9)						
Pituitary adenomas (6)	1	3	2	..	2	4
Other pituitary tumors (2)	2	..	..	1	1	..
Nasopharyngeal (1)	1	..	..	..	..	1
Parietal lesions (5)						
Meningioma, left (1)	1	..	..	..	..	1
Subdural hematoma (2)	2	..	..	..	1	1
Gliosis, precentral (1)	1	..	..	..	1	..
Encephalomalacia (1)	1	..	..	..	..	1
Vascular diseases (9)						
Angiospasm, right anterior choroid artery (1)	1	..	..	..	..	1
Circoid angioma, right internal carotid artery (1)	1	..	..	..	..	1
Ruptured aneurysm, middle cerebral artery (1)	1	..	..	1	..	..
Thrombosis, middle cerebral artery (1)	1	..	..	..	..	1
Migraine (2)	1	..	1	..	1	1
Aneurysm, left cavernous sinus (1)	..	..	1	1	1	..
Vascular syphilis (1)	1	..	..	..	1	..
Cerebral hemorrhage (1)	..	..	1	..	..	1
Multiple sclerosis (9)	7	2	..	..	2	7
Epilepsy (4)	3	..	1	..	2	2
Congenital paraplegia (1)	1	..	..	..	1	..
Toxic conditions (4)						
Bromidism (1)	..	1	..	..	..	1
Optic neuritis (3)	2	1	..	..	..	3
Hydrocephalus (2) (ages 21 and 34)	..	2	..	..	1	1
Optic atrophy (3) (nonsyphilitic)	..	3	..	..	3	..
Cerebellar astrocytoma (1)	1	..	..	..	1	..
Totals	29	12	6	2	18	27

B. Aids to Diagnosis Confirming Fields

Neurological Signs		Symptoms		Roentgenograms of Skull		Angiograms		Pneumoencephalograms		Electroencephalograms		Operation	
Positive	Negative	Positive	Negative	Positive	Negative	Positive	Negative	Positive	Negative	Positive	Negative	Positive	Negative
6	..	6	..	6	..	..	..	..	..	..	..	3	..
1	1	1	1	2	..	..	..	..	..	1	..	..	..
1	..	1	..	1	..	..	..	..	..	..	..	1	..
1	..	1	..	..	1	..	..	..	..	1	..	1	..
2	..	2	..	..	2	..	..	1	1	..	..	1	..
1	..	1	..	..	..	..	..	1	..	1	..	1	..
1	..	1	..	..	..	..	..	..	..	1	..	..	..
1	..	1	..	..	1	..	1	..	1	1	..	..	..
1	..	1	..	1	..	1	..	..	1	1	..	1	..
1	..	1	..	..	1	..	..	..	..	..	1	1	..
1	..	1	..	1	..	..	..	..	1	1	..	..	..
2	..	2	..	..	2	..	..	..	..	2	..	..	..
1	..	1	..	..	1	..	1	..	1	1	..	..	..
1	..	1	..	..	..	..	..	..	..	..	..	..	..
1	..	1	..	..	..	..	..	..	..	..	..	..	..
7	2	9	..	..	4	..	..	..	..	1	2	..	..
..	..	4	..	..	..	..	..	1	..	2	..	..	..
1	..	1	..	..	1	..	..	..	1	..	1	..	..
1	..	1	..	..	1	..	..	..	..	1	..	..	..
3	..	3	..	..	1	..	..	..	..	..	1	..	..
2	..	2	..	..	2	..	..	1	1	..	1	1	1
3	..	3	..	..	2	..	..	..	..	..	..	..	..
1	..	1	..	..	..	..	..	..	..	..	..	1	..

Figure 4 illustrates the fields of B. A., aged 45, who had a circoid angioma of the internal carotid artery near the right anterior clinoid process. He had attacks of sudden headache, nuchal stiffness, vomiting, weakness of the left arm, blurring, diplopia and memory loss. He showed vertical nystagmus on looking right, rotatory nystagmus on looking left and up, weakness of the left side of the face, hemiparesis and paresthesia of the left arm and leg and a positive Babinski reflex on the left. Roentgenograms showed calcification above and to the right of the anterior clinoid processes. The spinal fluid pressure was increased; caloric tests showed hyperactivity of the right labyrinth. Arteriograms revealed the angioma of the right internal carotid artery, and the electroencephalogram showed a minor disorder in the left

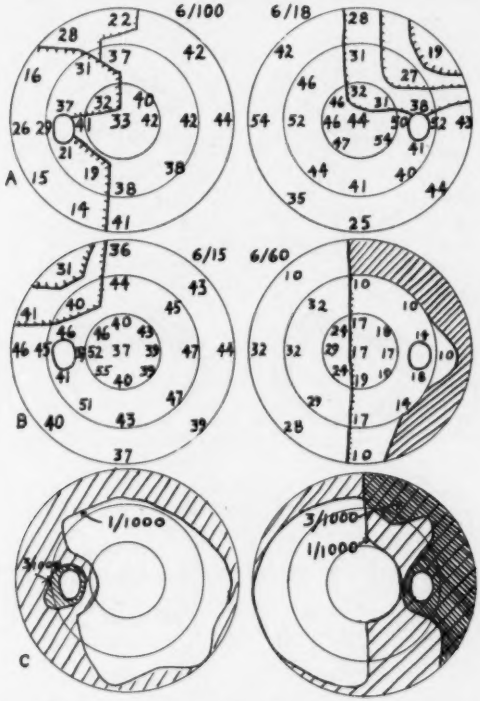

Fig. 3.—*A*, preoperative flicker fusion fields (Jan. 13, 1949) of C. B., aged 24, showing bitemporal loss. Standard fields (not shown) failed to suggest disease of the pituitary gland. *B*, flicker fusion fields (Feb. 2, 1949) after removal of tumor, which was attached to the right optic nerve sheath, and *C*, standard central fields (Feb. 7, 1949), both showing bitemporal loss.

frontotemporal area. Preoperative flicker fusion fields revealed definite complete left homonymous hemianopsia (fig. 4 *A*); standard fields, both central and peripheral (fig. 4 *B*), showed no hemianopsia. Postoperative fields, with improved visual acuity, showed persisting left homonymous hemianopsia in flicker fusion tests, but nothing at all with standard technic (fig. 3 *C*).

The data in the table on nine cases of multiple sclerosis are somewhat misleading because most of the fields were taken for this table during a visual remission. This was done to accentuate the fact that during the acute neuritis both types of field-taking technics show changes but that during a remission flicker fusion fields continue to show losses when standard fields become

normal. Flicker fusion fields also eventually improve. A striking difference in the fields was found. Where standard fields usually showed a centrocecal scotoma, flicker fusion fields showed also pronounced irregular peripheral changes. This is illustrated in the case of V. R., aged 24 (fig. 5). In *A*, taken during an acute episode, flicker fusion fields showed marked central and patchy peripheral loss in the right eye and moderate peripheral depression in the left eye. The standard central fields (fig. 5 *B*) showed the centrocecal scotoma in the right eye and no change in the left eye. Eighteen months later (fig. 5 *C*) the standard fields were normal and flicker fusion fields still showed irregular peripheral changes.

Figure 6 illustrates two cases of traumatic head injury in which standard fields were entirely normal but flicker fusion fields were useful in localizing the lesion. In the case of W. O., aged 38, the electroencephalogram indicated a focus in the right temporal area, and he had weakness

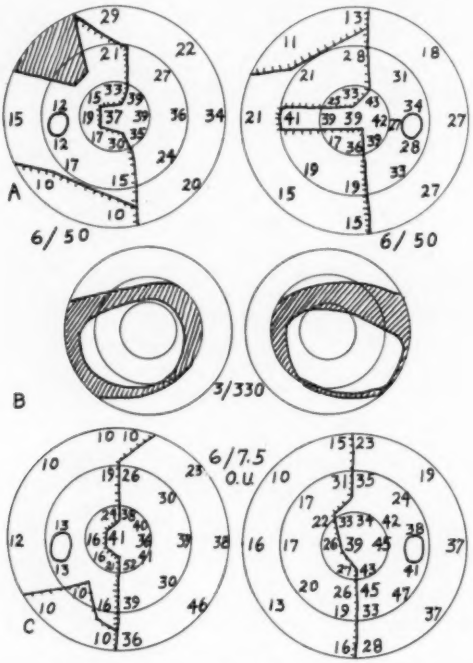

Fig. 4.—*A*, preoperative flicker fusion fields (March 1949) of B. A., aged 45, showing left homonymous hemianopsia due to circoid angioma of the internal carotid artery near the right anterior clinoid process. *B*, peripheral fields for 3/330 merely constricted (standard fields [not shown] were normal). *C*, postoperative flicker fusion fields (July 1949), showing even more decided hemianopsia, while standard fields showed no abnormality.

of the left side of the face and the left hand, impairment in the finger to nose test on the left and hypesthesia of the left cheek.

O. M., aged 55, had blurring spells and jacksonian attacks involving the right side of the face and abdomen. He had aphasia and astereognosis of the right hand, and the electroencephalogram showed mixed dysrhythmia and a focus in the left parietal area.

Optic neuritis of toxic origin, unlike that of multiple sclerosis, shows only central flicker field defects.

The fields of patients classified as epileptic in the table were recorded as more valuable with the flicker fusion technic, merely because the general and patchy depression was more pronounced in flicker fusion tests.

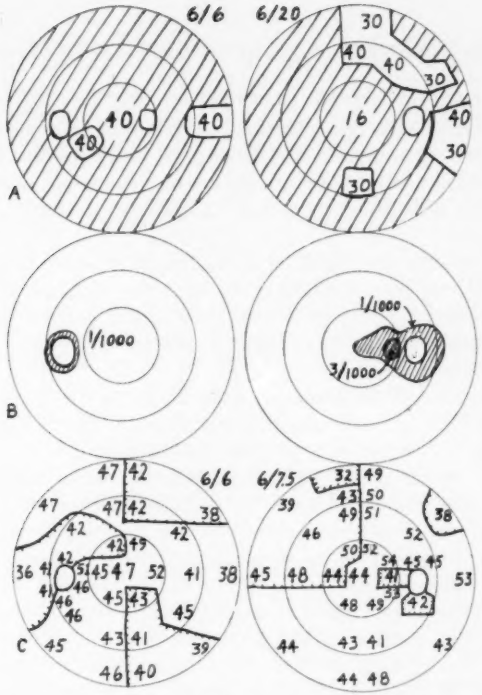

Fig. 5.—*A*, flicker fusion fields (old technic; June 1948) of V. R., aged 24, showing bilateral patchy central and peripheral depression. The patient had multiple sclerosis. *B*, standard central fields taken at the same time, normal except for the centrocecal scotoma of the right eye. *C*, eighteen months later (December 1949) flicker fusion fields, still showing patchy peripheral depression, while standard fields (not shown) were normal.

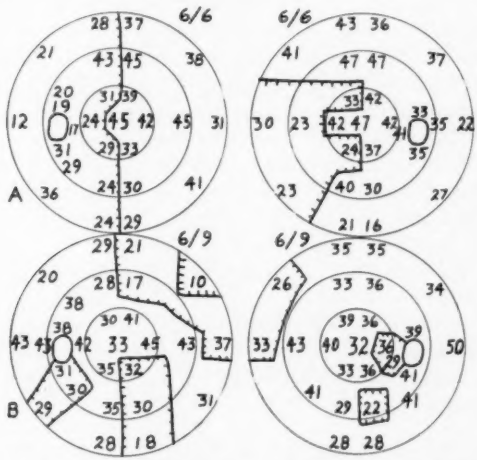

Fig. 6.—*A*, flicker fusion fields (September 1949) for W. O., aged 38, who had sustained a head injury five years before, for which he had been treated surgically. Although the standard fields were normal, the flicker fusion fields showed partial right nasal hemianopsia and complete left temporal hemianopsia, corresponding to the scar in the right temporal lobe. *B*, flicker fusion fields (December 1949) for O. M., aged 55, who had had a head injury four months before, with slight jacksonian attacks on the right. The standard fields were normal, but the flicker fusion fields showed partial nasal hemianopsia in the left eye, enlargement of both blindspots and one temporal defect in the right eye.

COMMENT

It is very certain that flicker fusion fields are superior to standard fields, particularly in patients with very early lesions or in those with such poor visual acuity that standard methods are unsatisfactory. Moreover, sick and confused patients unable to understand the technic frequently do better with the flicker fusion test.

Considering the physiology of flicker fusion frequency perception, this superiority is not surprising. An area of retina, given time, may respond to minimum light intensity, to minimum contrast or to form (test types) but will not recover soon enough after a flash stimulus to be able to respond to another following at the normal flicker fusion frequency.

Flicker fusion is a phenomenon of the light-adapted eye [9] and is higher with greater target brightness. The stimulus and response cycle, as expressed in the electroretinogram, is shorter with brighter flash stimuli, owing to the existence of a negative "A wave," which increases in amplitude with increasing brightness more than does the positive component, thus hastening electroneutrality, which apparently is necessary before response to a second flash is possible.

Flicker fusion frequency in the light-adapted eye is lowered in the fovea by inhibition reflexes and increased in the periphery by the effect of cone teamwork, where perhaps 16 rods and cones are represented by one ganglion cell. Suppose that one cone of this group responds to the first flash. A second cone is free to respond to the second flash, so that the same ganglion cell can transmit two distinct impulses 20 milliseconds or so apart. Experiments with interrupted electrical stimuli applied to the retina or optic nerve show that the visual pathways can transmit impulses with frequencies of from 100 to 160 per second [4] with conscious perception of flicker. Flicker fusion is a retinal phenomenon in the normal person. In spite of this, clinical flicker fusion tests show that intracranial visual pathways are easily injured, resulting in typical field defects.

When a foveal cone responds to a flash stimulus, the threshold of adjacent cones is raised (sensitivity lowered). Inhibition functions freely in the fovea, supposedly in the amacrine cells, which are particularly well developed there. Cerebral suppression, as seen in amblyopia ex anopsia,[10] functions chiefly in the fovea with relative peripheral immunity. The suppressed fovea has an increased flicker fusion frequency, due most probably to perception by the eccentric portion of the retina. A difference of central flicker fusion frequency of five flashes per second may be due to ocular dominance and be unimportant in interpretation of visual fields. Such a difference in the periphery would be significant.

Nevertheless, the normally low flicker fusion frequency in central vision may be attributed to inhibition processes. If a group of foveal cones respond to one flash stimulus, a second flash 10 milliseconds later results in perception of a single brighter flash, or summation. A second flash 50 milliseconds later results in perception of one weaker flash, or inhibition. A second flash 100 milliseconds later is perceived separately.

9. Miles, P. W.: Flicker Fusion Fields: II. Technique and Interpretation, Am. J. Ophth. **33**:1069-1077, 1950. Davson, H.: Physiology of the Eye, Philadelphia, The Blakiston Company, 1949, pp. 121-131.

10. Miles, P. W.: Flicker Fusion Frequency in Amblyopia ex Anopsia, Am. J. Ophth. **32** (June, pt. 2):225-230, 1949.

Refractive errors and translucent defects in ocular media have little effect on flicker fusion fields. Diffusion and dispersion may lower the light intensity, but at the same time image size increases, so that flicker fusion frequency remains constant.

The patient's age and pupil size have relatively little effect on flicker fusion fields in clinical usage.[11] Although the light-dark adaptive process deals with intensities 100,000 times the dark threshold, the pupil can change the intensity only 24-fold by constricting from 8 to 1.5 mm. in diameter. A small pupil reduces the flicker fusion frequency strikingly for about an hour, after which the flicker fusion frequency gradually returns to normal, in spite of the pupillary size. Many older patients in good health with small pupils were found to have normal flicker fusion fields; others showed slight uniform peripheral depression.

Flicker fusion frequency is not affected by fatigue or loss of sleep, nor is it influenced by training, as is the flash card recognition test. Flicker fusion fields are sometimes slightly depressed above and below the blindspots at the height of menstruation. During pregnancy there is regularly a bitemporal slant, due to physiological enlargement of the pituitary gland. Retinal vasospasm causes loss of sensitivity of adjacent retina.

Walker and associates[12] (1944) reported that flickering light annoys epileptic patients. A girl aged 17 had petit mal attacks when riding in an automobile along a lane of trees through which sunlight flickered. A woman aged 50 when tested with a flickering light became temporarily blind, then unconscious. A clerk aged 33 felt confused, then became unconscious without convulsion. Epileptics show greater than normal photic driving in electroencephalographic tests.[12]

SUMMARY AND CONCLUSIONS

Flicker fusion fields correspond in contour to those taken with standard methods but show more sensitivity, particularly in early cases, in which fields are most valuable. Of the 47 cases reported in this paper, flicker fusion fields were considerably superior to standard fields in 28 and slightly superior in 11 cases. In 23 of the cases, flicker fusion fields showed changes of localizing value when standard fields showed nothing. In no case was the flicker fusion field inferior to the standard field.

This superiority of visual fields obtained by testing flicker fusion frequency has been reported by other clinicians, and is to be expected on theoretical considerations.

Flicker fusion fields are practical and can be obtained quickly and accurately from sick and mentally disturbed patients. In most patients, flicker fusion fields can be taken by a technician in less than 15 minutes, with little chance of missing a slight defect. Interpretation is made by the clinician by a quick comparison of flicker fusion rates in the "paired areas" and with the normal field. The field defect in a given area is recorded as a number between 0 and 60; so the degree of visual loss is obtained without time-consuming tests with targets of different size and color.

640 South Kingshighway (10).

Members of the house staff and visiting physicians helped in gathering the clinical data.

11. Miles, P. W.: Flicker Fusion Fields: I. The Effect of Age and Pupil Size, Am. J. Ophth. **33**:769-772, 1950.

12. Walker, A. E.; Wolf, J. I.; Halstead, W. C., and Case, T. J.: Photic Driving, Arch. Neurol. & Psychiat. **52**:117-125 (Aug.) 1944.

LOBOTOMY AND PSYCHOPATHOLOGY

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AND
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THE EVALUATION of any form of therapy is fraught with difficulty. In psychiatry this is particularly true. Whether one of the physical therapies or a form of psychotherapy has been employed makes little difference. One cannot yet point to any universally acceptable general criteria having a high degree of predictive significance for the use of a given form of therapy in any given case.

There are many reasons for this, some of which derive from the nature of the problem and are quite similar to those encountered in general medicine. However, two features are outstanding: (1) a basic confusion in the concepts of "cause" and "cure" and (2) an astonishing lack of agreement between psychiatrists in their appraisal of the form and content of the behavior of their patients. It is the latter problem with which we are particularly concerned. Often two physicians cannot agree on what they see. Consequently, they cannot concur on the interpretations they make as to the effect of their therapy or its mode of operation. Oftentimes the major difficulty is one of language. They have not agreed on a system of symbols to represent what their senses and experience have taught them.

At present the literature is flooded with articles on lobotomy. Between the completion of this study and the actual writing of the paper two new books [1] have appeared dealing with the subject. Over the past few years well over 500 articles and reports have been published here and abroad, covering almost all phases of this method of treatment. In many instances the work has been well conceived and ably conducted, but psychiatrists have little basis yet for saying what will happen in a given patient with a specific disease when they use prefrontal lobotomy.

In 1947 Malamud and Sands [2] presented a clinical psychiatric rating scale designed to quantitate changes in a wide range of behavioral phenomena. In a later paper [3] they described the use of this scale in the study of the clinical effects of lobotomy in schizophrenic patients, derived in part from the application of this

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Dr. Reiner is Senior Physician, Worcester State Hospital
Dr. Sands was formerly Director of Research, Worcester State Hospital.

1. (*a*) Greenblatt, M.; Arnot, R., and Solomon, H. C.: Studies in Lobotomy, New York, Grune & Stratton, Inc., 1950. (*b*) Mettler, F. A.: Selective Partial Ablation of the Cerebral Cortex: A Correlative Study of Its Effects on Human Psychotic Subjects, New York, Harper & Brothers, 1949.

2. Malamud, W., and Sands, S. L.: A Revision of the Psychiatric Rating Scale, Am. J. Psychiat. **104**:231 (Oct.) 1947.

3. Sands, S. L., and Malamud, W.: A Rating Scale Analysis of the Clinical Effects of Lobotomy, Am. J. Psychiat. **105**:760 (April) 1949.

scale. Their experiences convinced them that this technic is valuable because it employs concepts sufficiently specific to allow common understanding among different investigators and because it permits a limited, but meaningful, quantification of observations. It was possible to quantify the behavioral changes in the psychosis, as well as the effects of lobotomy on the psychosis.

Not only does the present paper represent the written record of an isolated study, but it indicates the need for agreement among psychiatrists in describing the varieties of behavior and the terms used to describe them. We offer this study to encourage the development of better technics through trial and error. In the material to follow, we shall describe our technic for the study of the effects of lobotomy on a group of 31 psychotic patients. All patients were operated on by Dr. John T. B. Carmody, neurosurgeon at Worcester (Mass.) State Hospital, who used a method essentially that of Lyerly and Poppen.

MATERIAL AND PROCEDURE

The patients used in this study were those for whom lobotomy had been recommended by the regular staff of the hospital, independently of us. Once we were advised that a patient had been selected, we began the procedures to be described.

Eighteen women and 13 men constituted the series. The median age was 40, with a range from 23 to 62; and the median duration of psychosis was nine years, with a range of from 4 to 29 years. The diagnoses and their occurrence in the group were as follows: schizophrenia, 14 women and 10 men; manic-depressive psychosis, 1 woman and 2 men; psychosis with psychopathic personality, 1 woman and 1 man, and undiagnosed psychoses, 1 woman and 1 man.

This may not be considered an ideal group. It is representative, however, of the chronically psychotic population of state hospitals. Each patient was observed preoperatively for approximately two weeks, during which period clinical notes were made by the nurses and by one of us (E. R.) and at least two rating scales were determined. Postoperatively, each patient was rated every two weeks for eight weeks, and every six weeks for from 6 to 15 months, with an average follow-up period of 10 months.

In rating a patient, we attempted to judge the amount and kind of change occurring in a particular component of behavior. The present rating scale used consisted of 22 items. For purposes of any given study, not all items need be used. In this instance all were rated for purposes of obtaining a "total score," but detailed analysis of individual items was confined to only 15 of the 22. We omitted those items which were obviously noncontributory by inspection but included some for their intrinsic importance, rather than for any particular change.

We had, then, detailed records on 22 components of behavior of each of 31 psychotic patients who were observed preoperatively for two weeks and postoperatively for an average of 10 months. To ascertain the quantitative and qualitative changes in forms of behavior produced by the operation, we inspected each record and plotted changes in every component of the rating scale. We compared the average prelobotomy rating of each item for each patient with an average of the last two ratings made in the postlobotomy period. If too long a time had elapsed between the last two postlobotomy ratings, we used the final rating.

RESULTS OF STUDY

The results of the item analysis were studied for evidences of alteration from preoperative behavior in terms of the following possible changes:

1. The behavior returned to what was characteristic of the patient premorbidly.
2. The behavior was partially modified toward that existing premorbidly.
3. The behavior did not change appreciably.
4. The behavior altered radically, from one side of the scale to the other (cross-over); e. g., from depression to euphoria or from anorexia to omniphagia.
5. The behavior became more extreme, but in the same direction as before—e. g., from somber to depressed state or from mild anorexia to a state requiring tube feeding.

The following material has been abstracted from our item analysis:

1. *Appearance.*—Most patients were slovenly, untidy or incontinent preoperatively. Of these, about one-half showed return to normal habits or nearly so, and this proved to be a fairly good indicator of over-all improvement. An early return of interest in toilet habits and personal appearance may be regarded as a good prognostic sign.

2. *Motor Activity.*—Hyperactivity was more likely to be affected than underactivity. We believe that lobotomy reduces hyperkinetic activity and that when this change is observed after the tenth postoperative week it is a good prognostic sign. A few patients remained persistently underactive from the immediate postoperative period. This is a poor prognostic sign. Furthermore, underactivity prior to operation is unlikely to be altered by lobotomy and may become intensified.

3. *Mimetic Expression.*—The group contained patients who made extreme use of gesture and facial expression, as well as those who were impassive or "empty." We could find little evidence of any predictable effect of lobotomy on either type, unless the former was associated with general hyperactivity. Hyperactivity associated with grimacing and elaborate gesturing after lobotomy might be replaced by underactivity and stiffness of expression.

4. *Responsivity.*—Those who were isolated or resistive to any personal attention from others tended to become more responsive. This is not necessarily correlated with over-all improvement and may reflect merely an improved tolerance to persons within the hospital. Three such patients actually became worse, and two patients who previously tended to cling to others crossed over their base line and became isolated. If by the tenth week a patient shows a warm, friendly reaction to others, where previously he resisted attention, one may anticipate general improvement.

5. *Hostility Reactions.*—In an earlier study Sands and Malamud [3] found that usually strong extrapunitive tendencies were attenuated by lobotomy. Although some patients became even more destructive when there had been definite intrapunitive activity, reversals occurred, producing a patient who would now express his hostility outwardly. The present study in part confirmed this. We found most of our patients were rather extrapunitive, and, though this was reduced in 19 of 26, 2 were unaffected and 5 became worse. Of the 5 patients who were intrapunitive before operation, 1 was improved, but 4 remained the same. None crossed over to the opposite side. We also noted that improvement in hostility reactions was not correlated with general clinical improvement.

6. *Socialization.*—Whether a patient was previously withdrawn from group activity or forced himself into groups made little difference. After lobotomy there were various changes, without any specific pattern relating to the preoperative picture. Six patients previously meddlesome and disruptive in social groups became withdrawn and avoided such activities. The reverse of this was not observed. Ten patients after lobotomy showed what we called normal relationships to groups. We suspect that the remaining patients, regardless of their clinical picture immediately prior to operation, had never achieved a high degree of socialization, even before illness.

7. *Attention.*—When attention was withdrawn or showed "gaps" characteristic of schizophrenia, we found improvement in 13 of 21 patients. When the attention

defect was on the order of distractibility, six of 10 patients crossed over their base line and became preoccupied. This was associated with a poor outcome in four of the six who crossed the base line.

8. *Speech.*—Overtalkative patients became less so as a result of lobotomy, though, to have any prognostic significance, such a change must be correlated with other alterations of behavior. When it is not part of a more general hyperkinetic state, we cannot predict any change. A few patients even became undertalkative after operation.

9. *Associations.*—In contrast to item 8 (speech), in which we dealt essentially with the quantity of words produced, we are here concerned with qualitative aspects of the pattern of words produced. Since most of the patients were schizophrenic, we found the typical disturbances of associations—vagueness, tangentiality and irrelevancies—occurring rather uniformly prior to operation. After operation about one-half such patients showed improvement, and of these, six of 14 became normal. Those whose associations did not improve were consistently in the generally unimproved group. In four there developed association defects common to hypomanic patients, even though they had what were regarded as schizophrenic associations preoperatively. These four patients showed general symptomatic improvement. It is difficult to predict which schizophrenic patient will show improvement in associations. We are inclined to believe that factors outside the parameters covered by the rating scale, such as age, duration of illness and duration of hospitalization, are more important. Usually, however, when morbid associations were favorably influenced, general symptomatic improvement occurred, and when they were not favorably affected, there was none.

10. *Mood.*—If a real mood disorder, particularly depression, is present, one may expect some improvement. Euphoric states are less responsive and may be unaffected by lobotomy. This general conclusion is based on only a few cases, but our observations concur with those of other investigators.[4] Our schizophrenic patients for the most part had no real mood disturbance. They were usually somber or indifferent in their outlook and rather characteristically showed a monotony or flatness in this parameter of emotion. Most of these patients became more labile, and nine could be considered as essentially normal, but in six there developed rather overoptimistic, somewhat euphoric attitudes. Nine patients who were previously rather euphoric became normal, but six of them were in the general group regarded as unimproved. We are inclined to believe, then, that a primary mood disorder of the depressed type will be favorably influenced by lobotomy but that euphoric states, even if modified, will not be accompanied with general improvement. The presence of some depression in schizophrenic patients is a fair prognostic sign.

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4. (*a*) Rothschild, D., and Kaye, A.: The Effects of Prefrontal Lobotomy on the Symptomatology of Schizophrenic Patients: A Survey of 100 Cases, Am. J. Psychiat. **105**:752 (April) 1949. (*b*) Frankl, L., and Mayer-Gross, W.: Personality Change After Prefrontal Leucotomy, Lancet **2**:820 (Dec. 6) 1947. (*c*) Peters, H. N.: Traits Related to Improved Adjustment of Psychotics After Lobotomy, J. Abnorm. & Social Psychol. **42**:383 (Oct.) 1947. (*d*) Freeman, W., and Watts, J.: Prefrontal Lobotomy: Survey of 331 Cases, Am. J. M. Sc. **211**:1 (Jan.) 1946.

11. *Affect.*—Since affective disturbances are fundamental, we were surprised to discover that only two patients in the entire series showed real improvement in this item. Nineteen patients showed no change. Five patients who were previously labile crossed over their base line and became emotionally cool or inadequate. Three patients previously rather inadequate became emotionally active in a shallow, silly manner.

12. *Feeling.*—In rating feeling, our scale deals mainly with evidence of tension in reaction to conflict rather than with all the subtle components of this item. It is a measure of anxiety when the patient deals with material significant to him. The patients were about evenly divided between those who ranged from phlegmatic to apathetic and those who showed obvious tension, and even panic. After lobotomy the entire group except for three patients were dull and apathetic. Of the series of 31, 14 who were previously apathetic remained there. Ten others who were tense and panicky initially crossed over and became phlegmatic or apathetic. We believe that lobotomy reenforces preexistent apathy or indifference and produces it when its opposite has been present.

13. *Perception.*—There are differing reports [5] on the prognostic significance of sensory projections in response to lobotomy, particularly auditory hallucinations. We often found a tendency for sensory projections to be responsive to treatment. Of all 17 generally improved patients, 9 returned to normal from a hallucinatory or pseudohallucinatory condition. The condition of 6 others was favorably modified, but the hallucinatory experiences were not eliminated. Of the 17 patients, only 1 failed to show improvement in this category. Of all the 14 generally unimproved patients, the hallucinatory state of 11 was unchanged, and that of 3 was made worse. Only 2 of the 14 showed a favorable but partial modification of their sensory projections.

14. *Thought Processes.*—The fundamental disturbance in the logic of the patients' ideas is probably unimproved after lobotomy. The illogical or paralogical patient tends to remain so after operation. The paralogical reasoning is less generally conspicuous after operation, and it occurs mainly when the patient is under stress. If he has been rendered apathetic by the operation (item 12), one may then find a patient who seemingly cannot be upset by discussion of conflict material and therefore one who no longer shows much in the way of real disturbance in thought processes. Thirty of the 31 patients in this series had preoperative alogical or paralogical thinking, the exception being a patient in whom obsessive thought was most conspicuous. Of the 30 patients, 20 had less conspicuous defects in thought processes after operation. Those unaffected by lobotomy in this respect were 10 generally unimproved patients.

15. *Subjective Reorganization.*—This category is concerned with the contentual elements—with the apperceptive content rather than with how it is expressed. We found that projections are not necessarily unaffected by lobotomy. Nine patients with frank delusions showed very good improvement; seven showed some change; eight showed no change, and two became worse. Three patients who previously had morbidly internalized preoccupations crossed over to the opposite

5. Greenblatt, Arnot and Solomon.[18] Peters.[4c] Freeman and Watts.[4d]

side of the rating scale and exhibited externalized delusional trends. We may say that delusional content can be altered after lobotomy and that when this change occurs it is a good prognostic sign.

COMMENT AND CONCLUSIONS

Our series of cases and this study are not definitive for the evaluation of lobotomy. However, we have employed a method potentially useful for this purpose, and one which, if generally employed, would lead to more uniform criteria for handling the problems involved.

No one is really satisfied with current psychopathological terminology. This situation demands more empirically oriented investigations. Many workers have already recognized this, and an excellent beginning has been made. The rating scale employed in this study is proving a useful tool, and one that demands specific concepts and language for the definition of the behavioral phenomena described. One can now begin to state what kinds of behavior will be affected by lobotomy, and in what way, and what relationship these have to over-all improvement. Even with our relatively small number of patients, and these a chronic group, we can make certain statements about the effects of lobotomy on specific symptoms. From a review of our data, the following conclusions are reached:

In a group of chronic psychotic patients, one may expect general improvement in the condition in about 50 per cent, worsening in about 20 per cent and little change in the remaining 30 per cent. Of more importance are the responses of specific behavior patterns. Certain traits respond favorably to lobotomy; among these are untidiness, anxiety and depression. When there are mobilizable affect and verbal productivity, improvement may be expected after lobotomy, even in the presence of projections and paralogical thought. The nature of the improvement is another important aspect. One may have a relatively peaceable, cooperative patient, but with "the fight gone out of him." One type of defect may have been substituted for another, which is organic and permanent.

The affect and feeling are usually adversely affected by lobotomy in the direction of flatness and apathy. The patient with distractibility of attention may have a poorer prognosis than the patient with gaps of attention. We cannot anticipate a real change in the form of the patient's thinking, and delusional content is not necessarily a contraindication or an unalterable phenomenon.

SUMMARY

We have demonstrated how the Malamud-Sands clinical psychiatric rating scale may be used in evaluation of the effects of lobotomy on the psychopathology of a group of 31 psychotic patients. Their analysis revealed that certain behavior patterns were favorably, and others were adversely, affected. Certain phenomena regarded by some investigators as unalterable were found to be influenced by this treatment.

VALUE OF CONVULSIVE THERAPY IN JUVENILE SCHIZOPHRENIA

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IN GENERAL, the occurrence of psychoses of any sort during childhood has been considered infrequent. Although classic dementia precox is thought of as a disorder taking its origin during puberty and adolescence, individual cases of this disease developing during the period of childhood are still reported as clinical curiosities. In recent years, however, with the growth of genetic-dynamic concepts in psychiatry, and with the emphasis on mental hygiene in child guidance clinics, increased interest has been manifested in the study of psychoses during childhood. More and more reports and monographs have appeared in the literature dealing with childhood psychoses, especially the functional psychoses, such as schizophrenia; and, in spite of the fact that psychoses in children and juveniles are still rarely diagnosed as such, childhood schizophrenia is now recognized as a definite clinical entity. This, according to Bender,[1] "reveals pathology in behavior at every level and in every area of integration or patterning within the functioning of the central nervous system, be it vegetative, motor, perceptual, intellectual, emotional or social. Furthermore, this behavior pathology disturbs the pattern of every functioning field in a characteristic way. The pathology cannot, therefore, be thought of as focal in the architecture of the central nervous system, but rather striking at the substratum of integrative functioning or biologically patterned behavior." The reason for the difficulty in detecting early psychoses in children seems to be two-fold. First, the symptomatology of psychoses in childhood is not as sharply defined as it is in adults, and, second, such children and juveniles are as a rule first examined by the general practitioner, pediatrician and psychologist, who frequently consider the child's or the juvenile's bizarre reactions merely in the light of ordinary behavior problems and antisocial acts. Both the diagnosis and the treatment are centered around the individual symptoms without recognition of the implications of the deeper personality changes involved.[2] Thus, it is not at all surprising that frank major psychoses in persons under 18 years of age are rarely encountered in psychiatric hospitals for adults and in state institutions for the mentally ill.

From the Eastern State Hospital.

Presented at the Twenty-Seventh Annual Meeting of the American Orthopsychiatric Association, Atlantic City, N. J., Feb. 22, 1950.

1. Bender, L.: Childhood Schizophrenia, Nerv. Child. **1**:138, 1942.

2. Lurie, L. A.; Tietz, E. B., and Hertzman, J.: Functional Psychoses in Children: Analysis of Findings in 20 Cases of Psychotic Children Studied at Child Guidance Home, Am. J. Psychiat. **92**:1169, 1936.

Statistics concerned with the incidence of psychoses in children come mainly from child guidance centers and institutions dealing primarily with juvenile patients. According to a study made at the Child Guidance Home in Cincinnati by Lurie, Tietz and Hertzman,[2] the incidence of psychoses among an unselected group of 1,000 children was 2 per cent. In contrast to this, Kanner,[3] at the Johns Hopkins Hospital in Baltimore, reported an incidence of only approximately 0.25 per cent of psychoses among children, while at the Bradley Home in Providence, R. I.,[4] it was found that approximately 1.5 per cent of all children examined were suffering from major psychoses, chiefly schizophrenia.

With regard to statistics coming from psychiatric hospitals for adults, Strecker,[5] in Philadelphia, found only four schizophrenic patients under 15 years of age in a total of 5,000 admissions, while Kasanin and Kaufman [6] found 21 schizophrenics among 6,000 consecutive admissions to the Boston Psychopathic Hospital. Falstein [7] reported that 9 schizophrenics under 15 years of age were admitted to the Cook County Psychopathic Hospital in 1938 in a total of 1,711 schizophrenics of all ages and a grand total of 6,182 psychiatric patients of all types. Various other reports tend to confirm the general impression that frank major psychoses in persons under 18 years of age are rarely encountered in institutions for the mentally ill.

All workers in this field seem to agree that when a functional psychosis, especially schizophrenia, occurs in juveniles, it is potentially chronic, tending to run a malignant, and sometimes catastrophic, course. To quote Bradley,[4] "In spite of some apparently good results and favorable signs, the prognosis of childhood schizophrenia must, for the present, remain extremely grave."

There seemed to be ample evidence that the patient with a so-called juvenile psychosis, especially juvenile schizophrenia, did very poorly in the older state hospital, with its purely custodial approach; but new hope was held for the patient of this type with the advent of the new therapies, particularly convulsive shock, which has certainly proved a boon to state hospital psychiatry, has provided impetus to therapy and has proved a weapon to be administered hopefully and rather generally.

PRESENT INVESTIGATION

The present study is an attempt to evaluate the effect of convulsive therapy in cases of juvenile schizophrenia. All patients with a diagnosis of one of the schizophrenic reaction types and who entered Eastern State Hospital before they were 18 years of age were included in this study. Altogether, since the opening of Eastern State Hospital in 1891, 14,858 patients have been admitted. Of these, 291 patients were hospitalized for the first time when 18 years of age or younger. Their hospital records, as well as their follow-up records, were carefully checked and the data organized as to diagnosis, treatment, adjustment during hospitalization and readjustment in society after release. Special attention was paid to the treatment given, and, when needed, additional information was obtained through personal interviews, as well as by means of questionnaires in which specific data were sought, especially in regard to the patient's adjustment after release from the hospital.

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3. Kanner, L., cited by Lurie and others.[2]

4. Bradley, C.: Schizophrenia in Childhood, New York, The Macmillan Company, 1941.

5. Strecker, E. A.: Psychoses and Potential Psychoses of Childhood, New York M. J. **114**:209, 1921.

6. Kasanin, J., and Kaufman, M. R.: A Study of Functional Psychoses in Childhood, Am. J. Psychiat. **9**:307, 1929.

7. Falstein, E. I.: Psychoses in Children, Illinois M. J. **76**:271, 1939.

At this point, however, it should be mentioned that at Eastern State Hospital there have been no special facilities, in particular, wards and departments, assigned for the use and treatment of these juvenile psychotic patients, and thus, regardless of age and diagnosis, all patients coming into this institution have received essentially the same examination on admission, treatment and other routine measures. In other words, a patient who, for instance, was 12 years of age at the time of admission to the hospital was placed in a ward with patients 35, 50, 75 and even 90 years of age. This juvenile patient has eaten in the same dining room, participated in the same daily routine and been constantly subjected to the beneficial or detrimental influence of other patients, for the most part the adult mentally deranged. There have been no special provisions for continuation of schooling or manual training other than those during recent years, in the occupational therapy department and, very recently, in the music therapy department and the book bindery, to which, unavoidably, patients are still assigned to a considerable extent without attempt at classification or segregation on the basis of age.[8]

The 291 juvenile patients who were 18 years of age or younger when admitted for the first time to Eastern State Hospital represent an incidence of 1.97 per cent of the total admissions. Of this number, 187 (63 per cent) were males and 104 (37 per cent) were females. Of this group, 103 patients had a diagnosis of schizophrenia, an incidence of schizophrenia of 36 per cent among all juvenile patients. This is somewhat higher than the percentage of schizophrenic patients among all admissions to this institution, which was only approximately 28 per cent. Of the total of 103 juvenile schizophrenics (patients who were 18 years of age or younger when first admitted to Eastern State Hospital), none was under 10 years of age, 4 were between the ages of 10 and 12 years, 14 between the ages of 12 and 15 years and 85 between the ages of 15 and 18 years. Of this total of 103 juvenile schizophrenics who were admitted to the Eastern State Hospital since 1891, 47 had received considerable in the way of shock and other special therapies—prolonged narcosis; convulsive shock with picrotoxin, metrazol® and the electric current; insulin shock therapy, and narcosynthesis—and with one exception, these 47 juveniles receiving the newer therapies were chosen from juveniles received at the hospital since 1936, the time when convulsive shock therapies were started at this institution. Certainly, the types of shock treatment given these patients, especially in the beginning, have varied with the changes in prevailing opinion and the development of convulsive therapy as such; in other words, in the beginning the first patients of this group received only insulin shock therapy, whereas later, with the introduction of metrazol® shock, this type of treatment was chiefly used, and, more recently, with the advent of electric convulsion shock, this therapy has constituted the prevailing type. However, because of the continuous favorable reports in the literature on insulin shock, this type of treatment has been used all along, whereas metrazol® shock has not been given to any extent during recent years. In general, it may be said that most patients have received two types of convulsive therapy—mainly electric and insulin shock, or metrazol® and insulin shock—and if a patient was given only one type of convulsive therapy, this type was insulin shock. In addition, all the patients have also received the generally recommended adjunct therapies, such as psychotherapy, occupational therapy and recreational therapy, as well as other special treatments specifically indicated.

The present study, then, concerns itself with the 47 patients whose condition was diagnosed as one of the schizophrenic reaction types and who received intensive convulsive therapy. Eleven of the patients had at least one full course of electric shock therapy, consisting of from 15 to 20 treatments, and all but one of this group, in addition, received a full course of insulin shock treatment; 17 of the patients were given at least one course of metrazol® shocks, consisting of 10 to 15 such treatments, and 12 of this group also received an additional course of insulin shock treatment, while 19 patients received insulin shock therapy only, thus making 41 of the 47 who have received insulin shock only, or insulin shock in combination with either metrazol® or electric shock. It should be stated here that the insulin shock therapy was given five times a week for approximately 13 weeks and the patient was left in deep coma for approximately one hour during a treatment.

8. Perry, H. A., and Levy, S.: Juvenile Patient in the State Hospital, Dis. Nerv. System **11**:111, 1950.

The results following the treatment were classified as good, fair and poor. "Good" means the ability of the patient to leave the hospital after completion of the treatment and to make a permanent satisfactory extrainstitutional social adjustment. "Fair" means that the patient made a recovery from his acute psychotic episode under the treatment, so that he was able to be released from the hospital on parole; however, his extrainstitutional adjustment was not permanent and sooner or later he again showed evidence of his mental illness, necessitating return either to this or to some other institution for the mentally ill for another course of treatment. "Poor" indicates that although there may have been slight improvement under treatment, the patient soon again showed evidence of psychosis and was not able to be released from this institution, continuing as a patient here and showing a gradual downhill course in his mental illness.

Results.—This study revealed that in only six of the 47 patients receiving convulsive therapy could the results be considered as good; i. e., the patients responded to shock therapy and were able to be released from the institution and to make a permanent satisfactory extrainstitutional social adjustment. All six patients received insulin shock; in addition, two received electric shock. This, then, would indicate a recovery rate of 12.6 per cent for juvenile schizophrenic patients receiving convulsive therapy. For 10 patients, or 21.5 per cent, the results were considered as fair to poor, since these patients, after a temporary period of extrainstitutional adjustment, again reverted to their psychotic behavior and had to be returned to this or another institution for the mentally ill for further treatment. The remaining 31 patients, or 65.9 per cent, did not receive any benefit whatsoever from the various types of convulsive therapy. These results are in sharp contrast to those obtained in the total population at this institution, now exceeding 2,100, and therefore preponderantly an adult population. During recent years in the latter group approximately 31 per cent of all schizophrenic patients selected for various types of shock treatment responded favorably to such therapy, as compared with 12.6 per cent in the juvenile schizophrenic group.

This group of 47 juvenile schizophrenics who received convulsive therapy was then compared with the group of 56 juvenile schizophrenics who were received at this institution before the era of shock treatment and who received no treatment other than institutional care and some type of occupational therapy.

It is interesting to note that many of the patients in the untreated group have been discharged and that nine of the 56 patients have made a complete recovery; thus, the results being classified as good, the incidence would be 16 per cent. Twelve, or 21.4 per cent, have been released at one time but later had to be returned to this or another institution, the results being classified as fair, while in 35, or 62.6 per cent, of the patients the results were poor, since they are either still hospitalized here or have died in the meantime at this institution.

COMMENT

From the results of this study the conclusion seemed justified that schizophrenia when occurring before the age of 18 years appears to be potentially chronic and tends to run, with rare exceptions, a rather malignant course. This opinion was expressed in the older literature, but after the advent of convulsive therapy more hope was held for this type of patient, especially since the convulsive therapies have produced a better prognosis in adult schizophrenia. Apparently, however, the expectation that the newer therapies, mainly the convulsive therapies, could influence

favorably the course of juvenile schizophrenia has not been fulfilled; the general consensus in the literature, as aptly summarized by Bradley,[4] is that "all careful students of schizophrenia, as it appears in children, report a uniformly gloomy prognosis regardless of treatment. Except in rare cases therapy appears to benefit isolated symptoms only" and, furthermore, that "failure to respond to all forms of treatment is so conspicuous in childhood schizophrenia as to justify its being considered, for the present, a characteristic of the disease." In this connection, it is interesting to note that even with the newest methods of treatment, such as prefrontal lobotomy, the results in cases of childhood schizophrenia were also uniformly poor; but the proponents of this therapy still justify its use, for, according to them, if unchecked, schizophrenia in childhood would progress to complete decadence of personality.[9] On the other hand, although in the minority, some authors, especially Bender [10] and Despert,[11] claim that the prognosis in childhood schizophrenia is by no means uniformly as poor as reported heretofore in the literature.

As to the response of juvenile schizophrenics to shock treatment, Kalinowsky and Hoch [12] stated that "it is a general consensus that schizophrenic patients below the age of 15 do not respond well, and spontaneous and shock treatment recovery rates are low. The majority of these patients derive only temporary benefit from treatment and are inclined to relapse." The results of the present study are certainly in complete agreement with these authors, since only 12.6 per cent of the patients receiving intensive convulsive and other adjunct therapies made a complete recovery, in striking contrast to the 31 per cent of adult schizophrenics who after receiving the same types of treatment made a similar complete recovery. Furthermore, the recovery rate for juvenile schizophrenics before the advent of shock therapy appeared to be higher than the rate obtained with convulsive therapy. In the former group 16 per cent of the patients made a complete recovery, while, as mentioned before, in only 12.6 per cent of the treated patients were correspondingly favorable responses accomplished. Therefore, the conclusion seemed justified that juvenile schizophrenia does not appear to be influenced by the newer methods of treatment, such as the convulsive therapies, as reported in this paper, and apparently also not by psychosurgery, as reported by other investigators. This result is in sharp contrast to that for adult schizophrenia, which is said to respond favorably to these newer therapeutic measures. Although it is beyond the scope of this presentation to explain the extremely poor prognosis and the poor response of juvenile schizophrenia to the newer methods of treatment, especially convulsive therapy, one cannot but speculate, although this might become a controversial subject, whether or not the juvenile type of schizophrenia represents a disease entity entirely separate from adult schizophrenia. Certainly, as shown in this paper, the response to treatment and the prognosis are entirely different from those of the adult type,

9. Freeman, W., and Watts, J. W.: Schizophrenia in Childhood: Its Modification by Prefrontal Lobotomy, Digest Neurol. & Psychiat., Institute of Living **15**:202, 1947.

10. Bender, L.: Childhood Schizophrenia: Clinical Study of 100 Schizophrenic Children, Am. J. Orthopsychiat. **17**:40, 1947.

11. Despert, J. L.: Early Recognition of Childhood Schizophrenia, M. Clin. North America **31**:680, 1947.

12. Kalinowsky, L. B., and Hoch, P. H.: Shock Treatments and Other Somatic Procedures in Psychiatry, New York, Grune & Stratton, Inc., 1946.

and also, according to the literature, the symptomatology differs widely from that of the adult type. Furthermore, at least clinically, the juvenile type of schizophrenia has much in common with the type of schizophrenia manifesting the first, but insidious, development of symptoms during the involutional period of life. Although it is well known that both the adolescent and the involutional period are crucial periods for the development of mental illness, especially schizophrenia, the influence of these two types of disease of the endocrine glands, mainly the sex glands, can, of course, only be surmised. Factors which, at least clinically, the juvenile and the so-called involutional type of schizophrenia have in common are the malignant course of the illness and the extremely poor response to the newer therapies, while the so-called adult schizophrenia, occurring after adolescence and before the involutional period, does not appear to run such a rapid and malignant course and seems to respond much more favorably to treatment. The existence of juvenile schizophrenia as an entity, however, is only speculation, but the subject appears to be noteworthy and certainly warrants further investigation, especially in view of the fact that, according to Kalinowsky and Hoch,[12] "up to the present time, the main contributions in the field of organic therapy of the psychoses have been made by clinicians and demonstrate convincingly the importance of clinical research in psychiatry."

CONCLUSIONS

On the basis of the present study, the conclusion seems justifiable that the convulsion therapies do not appear to influence the course of schizophrenia when occurring in patients before the age of 18 years. Juvenile schizophrenia tends to run a malignant course.

PNEUMOENCEPHALOGRAPHIC CHANGES FOLLOWING PREFRONTAL LEUKOTOMY (FREEMAN-WATTS TECHNIC)

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ALTHOUGH prefrontal leukotomy has been utilized as a psychosurgical therapeutic procedure since 1935, very little has been written about the organic changes which are observed in the brain following this procedure, and even less about observable roentgenographic changes to be seen with pneumoencephalography.

It is the purpose of the present paper (1) to describe the pneumoencephalographic findings in 19 unselected cases before and after prefrontal lobotomy for variable periods of up to 20 months following the surgical procedure, and (2) to correlate the pneumoencephalographic findings with observations in the few autopsies performed at this institution and elsewhere.

HISTORICAL REVIEW

In June 1936, Egas Moniz published the results of "prefrontal leucotomy" on 20 patients on whom he had operated since Nov. 12, 1935. It was his theory, as stated by Freeman and Watts,[1] that "to cure these patients we must destroy the more or less fixed arrangements of cellular connections that exist in the brain and particularly those which are related to the frontal lobes." The earliest procedure devised by Moniz and his collaborators consisted of the injection of minute quantities of alcohol into the subcortical white matter of the prefrontal area. Later they devised the "leukotome," which consisted of a hollow needle carrying a stylet toward the tip of which was a flexible wire loop or a cutting blade. With this instrument they cut four to six "cores" in each prefrontal region.

The first prefrontal leukotomy performed in the United States was done by Freeman and Watts,[1] who adopted the Moniz procedure with certain modifications three months after its publication. The operative technic of Freeman and Watts was essentially the same as that employed in the cases reported in the present study. It consisted of the placement of a burr hole, carefully planned, in the superior por-

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1. Freeman, W., and Watts, J. W.: Psychosurgery: Intelligence, Emotion and Social Behavior Following Prefrontal Lobotomy for Mental Disorders, Springfield, Ill., Charles C Thomas, Publisher, 1942; Prefrontal Lobotomy: Survey of 331 Cases, Am. J. M. Sc. **211**:1, 1946.

tion of the coronal suture on either side; a blunt dissector was inserted into the frontal lobe through this hole in a perfectly horizontal plane to a depth of 5 cm. The gray matter on the medial surface of the frontal lobe was carefully avoided if possible, and the anterior cerebral artery was thus also avoided. The dissector was then moved in a small arc in a perfectly vertical plane anterior to the tip of the frontal horn of the ventricle; thus the white matter in each frontal lobe was cut in this vertical plane of the coronal suture. After each incision was made in the frontal lobe, it was irrigated with saline solution until the returning fluid was clear. According to Freeman and Watts, bleeding should usually be minimal.

METHOD OF STUDY

Between Oct. 25, 1945 and March 22, 1949, 83 patients at the Veterans Administration Hospital, North Little Rock, Ark., had prefrontal leukotomies; there was a total of 85 operations, as two patients had two operations each. Dr. Robert Watson, neurosurgeon, Little Rock, Ark., consultant to the hospital, performed all the operations. From May 21, 1947 to July 15, 1948 every patient but one had a pneumoencephalogram prior to the prefrontal leukotomy. This represented a total of 32 patients. Three of these patients had two pneumoencephalograms prior to operation. Postoperative pneumoencephalograms were obtained on 19 of these 32 patients. The 19 patients represented an unselected random sample dictated by feasibility alone. (It is a requirement of the Veterans Administration that a permit consenting to encephalography be signed by the next of kin of incompetent patients. Only 19 permits could be obtained among the 32 patients who had had preoperative studies.)

The preoperative pneumoencephalograms were usually obtained several days prior to operation, or at least within eight weeks. In one instance, however, there was an interval of nine months; in another, an interval of six months; and in three, intervals approaching three months. In no instance was a therapeutic procedure carried out between the time of the pneumoencephalographic study and the operation.

The postoperative studies were done at any time from four to 20 months after the prefrontal leukotomy. All but three patients were studied after a postoperative period of at least six months had elapsed. Over one-half the patients were studied after an interval of one year or more.

The patients were all white men with the exception of one Negro, and their ages varied from 24 to 66 years, seven in this series being over 38 years of age. These patients all carried a diagnosis of some type of dementia precox, with one exception, a white man aged 38, who had had a manic-depressive psychosis, manic type, for 22 years. In each case the prefrontal leukotomy was done only on the recommendation of a "leukotomy committee," a board of psychiatrists who studied each case brought to their attention by the various ward surgeons. In each of the 19 cases the duration of the psychoses exceeded three years, with the one exception of a white man aged 54, who had a known psychosis for only nine months. In several cases the psychosis had been present 10 years or more. In 11 of these cases some form of shock therapy had been given, without a satisfactory remission, but in every case the shock therapy antedated the pneumoencephalographic study which preceded prefrontal leukotomy. The pneumoencephalographic changes seen after shock therapy are not known, but it is possible that some of the changes noted in our "control" films prior to prefrontal leukotomy were related to the shock therapy. Certainly, the high incidence of pneumoencephalographic abnormality visible in this "control" series of films prior to operation is noteworthy.

The psychiatric details are beyond the scope of this paper. No attempt has been made to evaluate clinical improvement or the psychiatric results which might result from this type of psychosurgery.

PNEUMOENCEPHALOGRAPHIC FINDINGS

Prior to Prefrontal Leukotomy.—In nine of the cases, the pneumoencephalographic findings prior to prefrontal leukotomy could be considered as normal or at the upper limits of normal. In six of these nine cases the pneumoencephalograms

were normal in every respect, whereas in three the ventricles were considered at the upper limits of normal by measurement.

In five cases, the ventricular system itself was normal, but there was an increase in the amount of air in the subarachnoid space surrounding the brain, accentuating the sulcal markings. In two of these five cases the increase was somewhat diffuse, whereas in the remaining three cases the increase in subarachnoid air surrounding the brain was rather localized in the frontal regions.

In the remaining five cases the following abnormalities appeared in the preoperative pneumoencephalogram: (*a*) slight, diffuse dilatation of the entire ventricular system, as well as an increase in the air around the cerebral cortex, 1 case; (*b*) fairly considerable dilatation of the entire ventricular system with no other manifestations of abnormality, 1 case; (*c*) slight dilatation of the left lateral ventricle only, with increased sulcal markings overlying the left cerebral cortex, 2 cases; (*d*) questionable slight dilatation of the anterior horns of the lateral ventricles only, 1 case. Otherwise the pneumoencephalographic findings were within normal limits.

Thus, approximately one-half the "control" pneumoencephalograms were essentially normal in every respect, and the other one-half revealed evidence interpreted as indicating some measure of cortical atrophy or cerebral gliosis. One patient whose pneumoencephalogram fell in the latter group also had a small area of calcification in the frontal lobe.

It is significant that in none of the cases were the sulcal markings obliterated, nor did the subarachnoid space surrounding the brain appear to be obliterated.

After Prefrontal Leukotomy.—For ease of comparison, the postoperative findings will be described in the same sequence of cases as that noted in the control group.

Of the nine normal cases, four showed definite, but variable, degrees of dilatation of all four ventricles, but usually the dilatation was greatest in the anterior two thirds of the lateral ventricles; there was also diffuse, or almost diffuse, apparent obliteration of the subarachnoid space overlying the cerebral cortex and between the cerebral hemispheres.

In one of the nine normal cases, ventriculograms, rather than encephalograms, were made, and the ventricles were found to be diffusely dilated. A large porencephalic cyst occupied one frontal lobe. In this case evaluation of the subarachnoid space surrounding the cerebral cortex was not possible, considering that ventriculography ordinarily does not yield as much information in this respect as does pneumoencephalography. In three of the nine normal cases, the sulcal markings were virtually absent, but the ventricles remained normal in size and no other changes were noted. In the last of the nine cases, the sulcal markings were absent only in a 10 cm. circle around the burr holes, but no other changes were noted.

Of the five cases in which there was some increase in the sulcal markings and the ventricles were normal prior to operation, the postoperative encephalogram in one showed diffuse dilatation of the four ventricles, most marked in the anterior one third of the lateral ventricles, and obliteration of the sulcal markings in a 10 cm. circle around the burr holes. In one there were diffuse dilatation of all the ventricles, most prominent in the anterior one half of the lateral ventricles; diffuse obliteration of the sulcal markings, and small loculations of gas in the right frontal lobe, suggesting several small porencephalic cysts. In one the film showed dilatation

of the frontal horns of the lateral ventricles, the other ventricles remaining normal, and diffuse obliteration of the sulcal markings, chiefly, however, over the parietal and occipital lobes. In the fourth case there were dilatation of the right lateral ventricle posteriorly only and obliterated sulcal markings around the burr holes. In the last of these five cases two operations were performed: Five months after the first operation the pneumoencephalograms showed dilatation of the left lateral ventricle only and slight diffuse obliteration of sulcal markings overlying the cerebral cortex. Eleven months after the second operation, and 16 months after the first operation, the pneumoencephalogram showed progressive dilatation, involving both

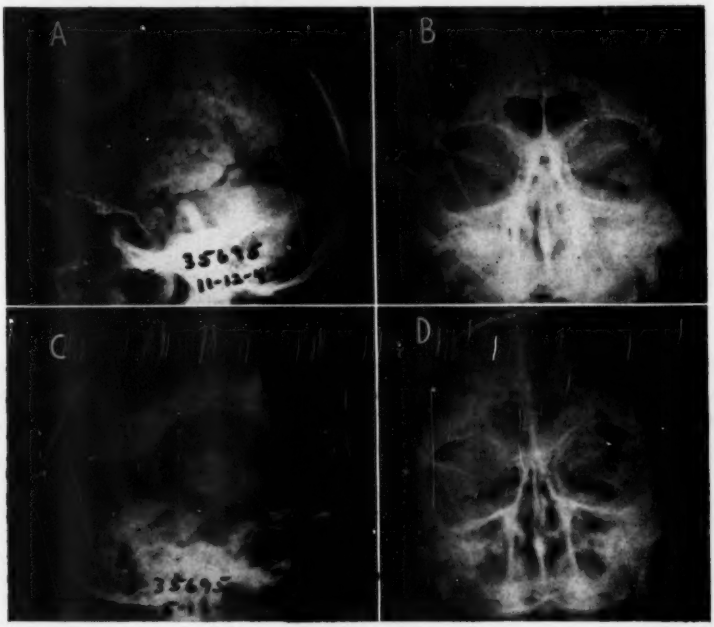

Fig. 1.—J. B., a white man aged 55, was hospitalized with the diagnosis of "delusions with alcoholic psychosis." The first pneumoencephalograms (*A* and *B*), taken on Nov. 12, 1947, showed a slight dilatation of the lateral ventricles and increased visualization of the sulci surrounding the brain, suggesting slight diffuse cortical atrophy and gliosis. There was also a very slight bulbous dilatation, particularly in the anterior horns of the lateral ventricle, suggesting a mild to moderate degree of cortical gliosis or atrophy of the frontal lobes. Prefrontal leukotomy was performed on Jan. 13, 1948, and the second pneumonencephalographic study (*C* and *D*), done on May 13, 1948, showed increased cortical atrophy and gliosis following the prefrontal leukotomy with evidence of a porencephalic cyst in the left frontal lobe. There was relative absence of gas in the subarachnoid space and sulci surrounding the brain and posterior to the burr holes.

lateral ventricles, and increased obliteration of the sulcal markings diffusely (fig. 1 *A*).

Of the two cases in which slight dilatation of the left lateral ventricle was evident only preoperatively and the cases in which sulcal markings were increased, one showed diffuse dilatation of the lateral ventricles, more prominent on the left, with a large porencephalic cyst in the left frontal lobe and diffuse diminution in the

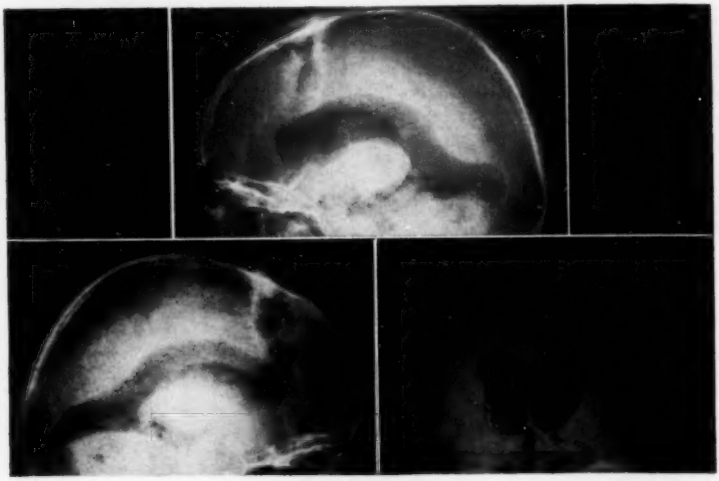

Fig. 2 (J. B.).—A third pneumoencephalographic study, performed May 23, 1949, showed progressively increasing cortical atrophy involving the entire brain diffusely, with a multiloculated porencephalic cyst, particularly in the left frontal lobe. The relative absence of air in the subarachnoid space surrounding the brain was noteworthy also.

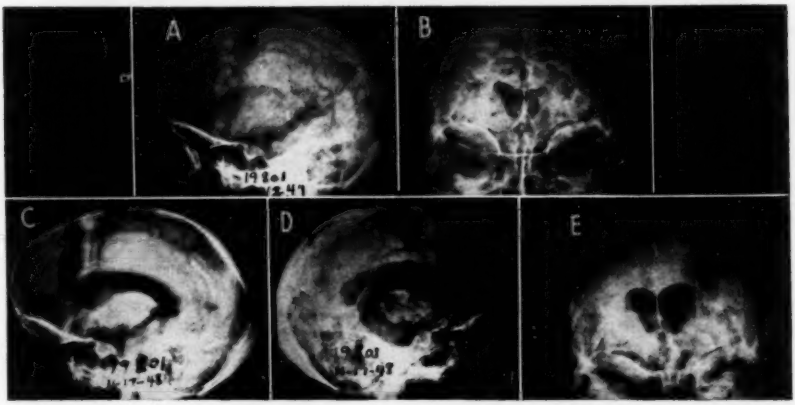

Fig. 3.—C. G., a white man aged 58, was admitted with a diagnosis of schizophrenic reaction, catatonic type. His first pneumoencephalographic study (*A* and *B*), performed on Nov. 12, 1947, showed dilation of the left lateral ventricle and diffuse increase in the sulcal markings overlying the entire brain. This suggested a cortical gliosis or atrophy, particularly in the left cerebral hemisphere. A perfrontal leukotomy was performed on Jan. 23, 1948. The second pneumoencephalographic study (*C*, *D* and *E*), performed approximately 10 months later, on Nov. 17, 1948, showed diffuse hydrocephalus with diffuse dilatation of the ventricles of the brain. There was also a relative absence of gas in the sulci surrounding the brain, suggesting that the hydrocephalus was of external origin. There was the new appearance of a porencephalic cyst communicating with the left lateral ventricle. It was thought that there was probably associated cortical gliosis and atrophy, particularly in the frontal lobes. It is perhaps significant in this instance that there is increased visualization of the basal cisterns and cisterna ambiens.

sulcal markings. In the other the findings were essentially similar, but the porencephalic cyst in this instance measured 6 by 4 cm. The obliteration of the sulcal markings, however, was considerably more pronounced, but there seemed to be increased visualization of the basal cisterns.

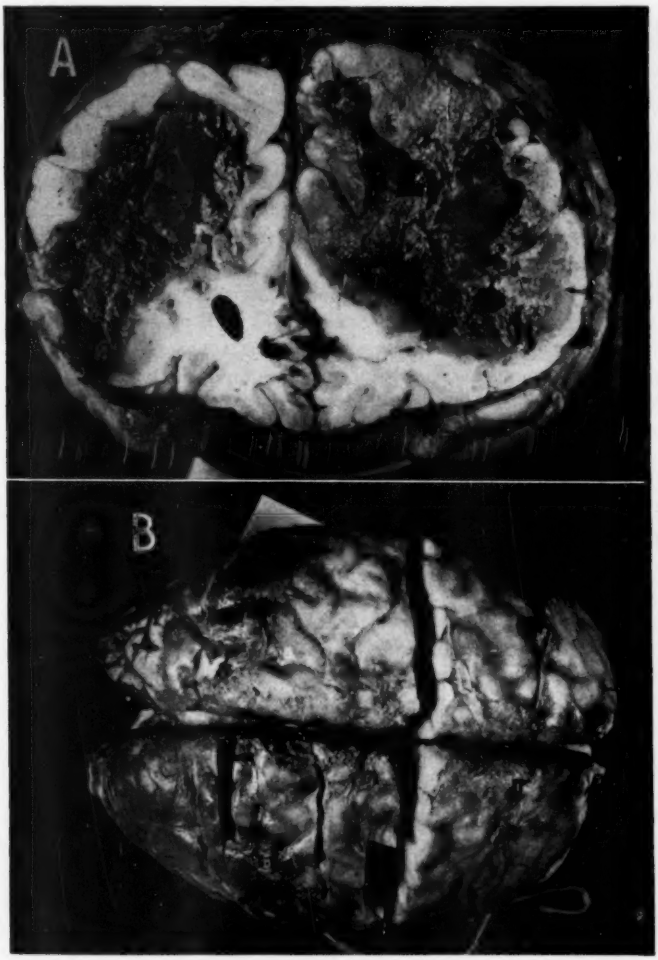

Fig. 4.—Brain of V. C. (table).

In the case in which the preoperative film had shown a slight diffuse dilatation of the entire ventricular system, as well as increased air in the sulcal markings around the cortex, two postoperative pneumoencephalograms were taken, with the following findings: Four months after the operation there developed increased dilatation of all the ventricles, greater on the left side; a porencephalic cyst, in the left frontal

lobe; obliteration of the sulcal markings posterior to the burr holes, and "puddling" of the sulcal markings over the frontal lobes. Sixteen months after the operation, and twelve months after the previous study, there was considerable progression of all these changes.

In the case in which considerable dilatation of the ventricles was evident preoperatively, with no other detectable abnormalities, there developed a further increase in the size of all the ventricles, particularly the lateral ventricles, and a porencephalic cyst measuring 6 by 3 cm., in the left frontal lobe, with no changes in the appearance of the sulcal markings.

In the case with a questionable slight dilatation of the anterior horns of both lateral ventricles preoperatively and a small area of calcification in the right frontal lobe the postoperative roentgenogram showed the least change of all. There had developed very slight dilatation of only the anterior horns of the lateral ventricles and an increase in the sulcar markings of the frontal cortex and anterior one half of the parietal lobes.

In summary, there were significant pneumoencephalographic changes in all the cases, regardless of the preoperative findings: (1) the progressive dilatation of all the ventricles, frequently most pronounced in the anterior portions of the lateral ventricles; (2) the progressive apparent obliteration of the subarachnoid space surrounding the cerebral cortex, seemingly the most prevalent finding, and (3) the development of porencephalic cysts, in five cases and possibly in a sixth, in only one of which the preoperative pneumoencephalogram was completely normal. The other four definite porencephalic cysts developed in cases in which the ventricles were dilated preoperatively, and hence the anterior horn of the lateral ventricle was very likely penetrated by the operative procedure.

RÉSUMÉ OF FIVE CASES WITH AUTOPSY AT THIS HOSPITAL

None of the patients in the present series died, but of all the patients at this hospital who have had a prefrontal leukotomy (85), seven are now dead and autopsies were performed on six. In one of these autopsies the examination of the brain was omitted; and in the others, it was somewhat abbreviated, in view of the fact that the pathologists at this hospital were required to send the brains to the Army Institute of Pathology, where a more extensive study is to be carried out in the future.

A brief résumé of the pathological changes in the brains of those patients on whom autopsies were performed at this hospital after prefrontal leukotomy may be presented, as follows (table): 1. Thickening of the arachnoid with varying amounts of grayish discoloration and opacity was found in all cases. 2. The cerebral cortex was definitely thinned in all but one case. There were also widening of the sulci and narrowing of the gyri. In one case there were also multiple areas of softening in the gyri. 3. There was slight to moderate dilatation of the ventricular system in all but one case. 4. In one case (with death two months after prefrontal leukotomy) a large porencephalic cyst was present in the left occipital lobe, with marked degenerative changes in the white matter in the frontal lobes and multiple cyst formation. In another case (with death 10 months after prefrontal leukotomy) there was also advanced cystic degeneration in the frontal lobes of the cortex, as well as in the

Pertinent Gross and Microscopic Changes in the Brain in Five of Six Cases Following Prefrontal Leukotomy Freeman-Watts Technic*

Patient	V. C.	E. H.	B. B.	E. R. H.	C. T.
Clinical diagnosis (psychiatric)	Meningo-encephalitic syphilis with psychosis	Paranoid psychosis	Dementia precox, hebephrenic type	Dementia precox, catatonic type	Syphilis of central nervous system, tabetic type
Major cause of death	Cardiac tamponade; pericardial hemorrhage from dissection between aorta and pulmonary artery at their origin	Acute hemorrhagic pancreatitis	(1) Bronchogenic carcinoma; (2) old tuberculosis; (3) coronary artery disease	Pick's lobar sclerosis involving frontal and temporal lobes; bronchopneumonia	Pulmonary edema; coronary artery disease
Interval between operation and death	12 days	49 days	4½ months	2 months	10 months
		Brain: Gross Pathologic Study			
Meninges	Arachnoid thick, gray and opaque	.....	Few small focal scars in arachnoid	Dura thick and dense and scarred over frontal lobe; arachnoid thick and slightly yellow	Definite but mild increase in thickness
Gyri and sulci	.....	Flattened and shallow	Frontal and temporal gyri narrowed and sulci widened and deepened	Widening of sulci and narrowing of gyri	Widening of sulci and narrowing of gyri
Cortex	Two sessile areas of cortex protruding through arachnoid under burr holes; cortex thinned everywhere	Cortex elevated under burr holes; shrunken and collapsed over cyst of occipital lobe	Cerebellar atrophy (on each side of flocculus); slight generalized atrophy	Marked atrophy and few areas of softening	Extreme atrophy; cystic yellow degeneration in frontal cortex
White matter	Almost complete replacement of frontal lobes by clotted blood; irregular cystic areas in basal ganglia, 1-1.5 mm.	Degenerated area at site of operation, with cyst formation (5 mm. anterior to frontal horn); porencephalic cyst of left occipital lobe	.....	Atrophy in basal ganglia; pineal gland large (5×4×4 mm.)	Cystic yellow degeneration in region of operative tracts
Ventricles	Displaced slightly to right with sanguineous cerebrospinal fluid	Posterior horn of left lateral ventricle dilated	Slight dilatation	Symmetric dilatation of entire ventricular system	Symmetric but somewhat enlarged
Evidence of hemorrhage	Generalized subarachnoid hemorrhage, especially posteriorly	.....	.....	Small areas of subdural hemorrhage at base of skull in left temporal and frontal fossae	.....
		Microscopic Observations			
Meninges	Hemorrhagic, thickened arachnoid	Thickened with cellular infiltration; considerable brain sand under pia; large number of phagocytic cells in area of leukotomy	†	Monocytes and macrophages with granular brown pigment	Slight increase in number of monocytes

Pertinent Gross and Microscopic Changes in the Brain in Five of Six Cases Following Prefrontal Leukotomy Freeman-Watts Technic—Continued*

Patient	V. C.	E. H.	B. B.	E. R. H.	C. T.
Cortex	Chromatolysis; thinning	Encephalomalacia in area of operation close to ventricles, with cyst formation, edema, lacunas and many gitter cells; thinned in occipital lobe with cyst formation and gliosis; chromatolysis, lacunas, satellitosis of neurons; arteriosclerosis	†	Thinned layers; disorganized increase in size of perineural spaces and perivascular spaces; cells showing chromatolysis and dark staining; patchy demyelination	Dilated perivascular and perineuronal spaces; chromatolysis of neurons; disorganization of layers; encephalomalacia
White matter	Lacunas; small areas of perivascular hemorrhage	.....	†	Increased glial fibers parallel to surface and wavy, patchy demyelination	Large areas of softening and degeneration; accumulation of gitter cells
Basal ganglia	Lacunas; basophilic granular material in vessel walls	Chromatolysis and perivascular rarefaction of tissue; satellitosis of neurons; sclerosis of small artery; granular basophilic material in walls of small arteries	†	Neurons shrunken and dark staining with dark brown granules	Sclerosis of walls of small vessels; some areas of rarefaction of tracts; chromatolysis of ganglion cells
Cerebellum	Lacunas; neurons of dentate nucleus shrunken and dark staining	Granular basophilic material in walls of small arteries	†	.....	Sclerosis of walls of small vessels
Hemorrhage	.....	.....	.....	Patches in cortex	.....
Miscellaneous data	Gliosis of optic nerve with large spaces present	Congestion and dilatation of perineuronal and perivascular spaces in hippocampus	.....	.....	.....

* The total number of cases in which this procedure was used was 85. Drs. E. Lloyd Wilbur, R. A. Burger and A. Nettleship made the pathological examinations.
† Data omitted; brain sent to Army Institute of Pathology.

subcortical white matter. Microscopic examination revealed the degenerative areas described above, and multiple microscopic hemorrhages in the white matter. In one case (with death two weeks after operation) small cystic areas 1 to 1.5 mm. in diameter were present in the basal ganglia. Basophilic granular material was noted in the basal ganglia, and the neurons of the dentate nucleus were shrunken and dark staining. In other cases, there was chromatolysis of the neurons with areas of disorganization of layers of the cortex and "drying out" of the neurons. The cortex showed a general reduction of cells.

In three of the cases with autopsy described above a clinical diagnosis of syphilis of the central nervous system had been made. The findings in these three cases can be related, at least in part, to syphilis of the central nervous system. However, the similarity of the findings in these cases with the other three cases and with the few cases with autopsy reported in the literature would indicate that at least some of the changes were due to the prefrontal operation.

RÉSUMÉ OF CASES WITH AUTOPSY REPORTED IN THE LITERATURE

A study of the literature reveals only a few cases in which autopsy has been performed and the case reported. In 531 patients operated on 610 times, Watts and Freeman [2] reported only 12 operative deaths (2.3 per cent). They reported two necropsies in detail, one performed six months and one less than one month after operation. Greenwood [3] reported a case with autopsy 35 months after operation. Meyer, Beck and McClardy [4] made special pathological studies on eight brains with prefrontal leukotomy, with emphasis on the tracts involved in the projection of these tracts onto the cortex. Meyer and Beck [5] studied nine cases with autopsy in another series.

All the reports, including those given in detail by Watts and Freeman, agree that the damage in the operative tract is moderately to extremely great. These other investigators also have found slight to severe cyst formation and traumatic cavitation, widening of the sulci and flattening of the gyri and, usually, moderate dilatation of the ventricles, as described in the present study. Almost always there are degeneration in the nucleus medialis dorsalis of the thalamus and degenerative changes in the basal ganglia. Freeman and Watts indicate that the latter changes are of paramount importance and deny the presence of any significant cortical atrophy. The other reports, however, indicate that cortical atrophy was found to some extent in all cases.

CORRELATION BETWEEN AUTOPSY OBSERVATIONS AND PNEUMOENCEPHALOGRAPHIC CHANGES IN PRESENT SERIES

Autopsy revealed a variable amount of arachnoidal and dural hemorrhage. infiltration and thickening. In three of our six cases this could not be evaluated, since it was partially due to syphilis; but in the other two cases arachnoidal hemorrhages and thickening and infiltration were also described. In correlation with this finding, the almost universal disappearance or absence of air in the subarachnoid space surrounding the cerebral cortex was a striking pneumoencephalographic feature. These findings would suggest one or both of two possibilities: (1) a relatively marked obliteration of the subarachnoid space over the cerebral hemisphere, as a result of the prefrontal leukotomy, or (2) obliteration of the communicating channels between the basal cisterns and/or the ventricles and the subarachnoid space overlying the outer surface of the cerebral cortex.

Either of these phenomena would result in a serious impediment to the absorption of the cerebral spinal fluid by the arachnoidal granulations. This disturbance. in turn, would cause an external type of hydrocephalus. The external hydrocephalus, in a variable degree, was indicated both in the autopsy findings previously described

2. Watts, J. W., and Freeman, W.: Prefrontal Lobotomy: Complications and Their Treatment, J. Internat. Coll. Surgeons **11**:343, 1948; Surgical Aspects of Prefrontal Lobotomy, ibid. **5**:233, 1942.

3. Greenwood, J., Jr.: Post-Mortem Findings in Prefrontal Lobotomy, Dis. Nerv. System **9**:279, 1948.

4. Meyer, A.; Beck, E., and McClardy, T.: Prefrontal Leucotomy: A Neuro-Anatomical Report, Brain **70**:18, 1947.

5. Meyer, A., and Beck, E.: Neuropathological Problems Arising from Prefrontal Leucotomy, J. Ment. Sc. **91**:411, 1945.

and in the pneumoencephalograms. Since the greater injury was in the frontal lobes, the more prominent dilatation of the anterior horns of the anterior one half of the lateral ventricles can be readily explained.

These signs of hydrocephalus are, in turn, correlated with the pathological evidence of cortical atrophy, sulcal widening and gyral flattening, which likewise would indicate some measure of cortical and cerebral atrophy. That these changes can be progressive is indicated by those studies that were performed serially on at least two occasions after operation.

BRIEF PSYCHIATRIC EVALUATION

No extended attempt has been made in this study to evaluate the clinical psychiatric changes in these patients which might result from the procedure. There was no correlation between the pneumoencephalographic changes following operation and the degree of clinical improvement noted.

It is perhaps significant to note that of the 19 patients studied here, only one has been permitted to leave the hospital as a well adjusted person. Nine others showed some measure of improvement but are still hospitalized. Usually this improvement meant that they were less combative and more docile or that they could be transferred to an open ward. The remaining nine patients have shown no psychiatric improvement.

SUMMARY AND CONCLUSIONS

Nineteen unselected cases in a series of 32 consecutive leukotomies were studied by pneumoencephalograms shortly before and up to 20 months after operation. The leukotomies were performed in accordance with the Freeman-Watts technic on patients with refractory psychoses of varying age groups.

The pneumoencephalographic changes in these 19 cases have been described in considerable detail. In nine of these the preoperative pneumoencephalograms were normal in all respects. In five of these nine cases postoperative studies showed diffuse dilatation of the ventricles, and in all of the nine there was a significant absence of air in the subarachnoid space surrounding the brain. In one case there developed a large porencephalic cyst, occupying almost all of one frontal lobe.

In five cases the ventricles appeared normal preoperatively, but there was an increase in the sulcal markings. Postoperatively the ventricles also showed progressive dilatation with obliteration of the subarachnoid space surrounding the brain. In one of these five a porencephalic cyst also developed. In the remaining five cases studied preoperatively there was diffuse or localized ventricular dilatation. In four of these there developed frontal porencephalic cysts, progressive ventricular dilatation and obliteration of the subarachnoid space surrounding the brain.

The related pathologic changes found in five of seven cases in which autopsy was performed were as follows: (*a*) cystic necrosis of the frontal lobes; (*b*) atrophy and gliosis throughout the brain; (*c*) meningeal thickening, scarring and hemorrhages; (*d*) generalized enlargement of the ventricles, most prominent in the frontal horns, and (*e*) cystic degeneration of the thalamus and basal ganglia, particularly in the nucleus medialis dorsalis of the thalamus.

The hydrocephalus described as a roentgenographic finding is probably due to a combination of cerebral gliosis and atrophy and a decrease in the absorptive

function of the arachnoidal granulations. It may also be related to some extent to obstruction to the free egress of spinal fluid between the basal cisterns and the subarachnoid space overlying the brain.

Porencephalic cysts occurred with greater frequency in those cases in which dilatation of the anterior horns of the lateral ventricles was present preoperatively, either as a localized dilatation or as a part of generalized enlargement of the ventricular system. We feel that this incidence is easily explained by the fact that the anterior horns of the dilated ventricles are more easily penetrated by the leukotome at operation.

These findings are consistent with those in the cases reported in the literature.

To prevent this occurrence, we suggest that pneumoencephalographic studies be included in the preoperative work-up in all cases of prefrontal leukotomy. In those cases which show dilatation of the frontal horn of the ventricle, the surgical technic should be modified accordingly.

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Dr. Robert Watson, neurosurgical consultant, permitted the use of these operative reports, and Dr. E. Lloyd Wilbur and Dr. Robert A. Burger, pathologists, and Dr. Anderson Nettleship, consultant in pathology, permitted use of the necropsy reports, in this series of cases.

VISUAL FUNCTION IN PERIMETRICALLY BLIND FIELDS

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IN NEUROLOGY, as well as in other branches of medicine, there is a tendency to classify function without stating the conditions under which it operates. Thus, when a patient is said to have a homonymous hemianopsia, a complete loss of all visual function in the anopic area is implied. This implication, however, is valid only for the conditions under which the examination is performed. A change in these conditions might lead to a different result, the apparent absence of function reflecting merely the particular set of conditions under which the function is examined.

In previous communications, it was demonstrated that perimetrically determined macula-splitting hemianopsias, when tested with the methods of tachistoscopy or visual after-imagery, may reveal preservation of vision in some of the defective areas.[1] On the other hand, the presence of function does not always imply complete preservation. Examination of fields of vision with such special methods as bilateral simultaneous stimulation [2] or visual flicker [3] may reveal defects in areas in which perimetry indicates apparently normal vision. In this communication we wish to report the visual reactions obtained in fields of vision which were apparently blind when examined by the standard perimetric method under daylight or 7 foot candles of illumination. We shall designate this type of field defect a perimetrically blind field.

MATERIAL AND METHODS

Eleven patients with visual field defects were studied. These defects were demonstrated by the routine perimetric method, using a 1 degree white target at a distance of 330 mm. and under 7 foot candles of illumination. In every case the retinas appeared normal on ophthalmoscopic examination. On the basis of clinical evidence, each patient was presumed to have a lesion in the optic pathways.

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This investigation was supported in part by a research grant from the National Institute of Mental Health, United States Public Health Service, and in part under contract #V1001M-176 with the United States Veterans Administration.

1. Bender, M. B., and Teuber, H. L.: Phenomena of Fluctuation, Extinction and Completion in Visual Perception, Arch. Neurol. & Psychiat. **55**:627-658 (June) 1946. Bender, M. B., and Kahn, R.: Visual After-Imagery in Defective Fields of Vision, J. Neurol., Neurosurg. & Psychiat. **12**:196-204 (Aug.) 1949.

2. Bender, M. B., and Furlow, L. T.: Phenomenon of Visual Extinction in Homonymous Fields and Psychologic Principles Involved, Arch. Neurol. & Psychiat. **53**:29-33 (Jan.) 1945.

3. Teuber, H. L., and Bender, M. B.: Critical Flicker Frequency in Defective Fields of Vision, Federation Proc. **7**:123-124 (March) 1948.

The accompanying table presents the pertinent perimetric and clinical data.

Routine perimetric studies were made on all patients under 7 foot candles of illumination, thereby demonstrating areas of blindness (i. e., perimetrically blind fields). After this, perimetric measurements were carried out in almost complete darkness.[4] The target was transmitted light exposed for short times, usually 1/25 second. The fixation point was a just visible pinpoint of red light. The head was immobilized by a jaw rest. One eye was covered while the other was tested. The targets subtended 20 minutes to 6 degrees of retinal angle and were placed at different points in the visual field. The source of light was a General Electric no. 55 clear bulb behind a milk glass screen, at which the intensity was measured in millilamberts with a

Perimetric and Clinical Data on Eleven Patients with Visual Field Defects

Case Initial	Age, Yr.	Perimetric Fields	Clinical History
1 A. F.	39	Left homonymous hemianoptic defect with 8° macula sparing	Right occipital subdural hematoma; right third nerve paresis (transient) Cause: presumably traumatic
2 M. F.	42	Left homonymous hemianoptic defect with 5° macula sparing	Right subdural hematoma, with transient, mild, right-sided paresis and bilateral hyperreflexia Cause: never clearly established; patient known alcoholic with rheumatic heart disease and signs of subacute bacterial endocarditis
3 R. F.	50	Complete blindness	Pituitary tumor; syphilis
4 A. M.	29	Bitemporal heteronymous hemianopsia with binasal 8° ring scotoma and 8° macula sparing	Six years of progressive visual difficulty, especially with night and color vision; no chiasmal lesion seen in pneumoencephalogram; defect in color vision in tests with pseudoisochromatic cards
5 E. G.	72	Right homonymous hemianopsia with 5° to 8° macula sparing	Elements of aphasia; occasional periods of confusion; no paresis but episodes of unconsciousness, with falls leading to mild trauma; hemianopsia after one such episode Cause: diagnosis of chronic hypertensive arteriosclerotic heart disease at death; no autopsy
6 M. E.	18	Right homonymous hemianopsia with 18° to 20° macula sparing	Sudden onset of homonymous hemianopsia, unaccompanied with other signs or symptoms Cause: unknown
7 H. G.	66	Bilateral, almost complete homonymous anopsia with some vision remaining to either side of midline of inferior quadrants of both visual fields	Sudden onset of dizziness, blindness and nonpsychotic visual hallucinations (1944); mild improvement in vision Cause: unknown
8 S. R.	30	Left peripheral homonymous hemianoptic field defect, which cleared spontaneously	Rheumatic heart disease in childhood; hemoptysis and transient left hemiparesis (1947); reprecipitation of left hemiparesis by carbon monoxide (1949), accompanied with left hemisensory syndrome and hemianopsia; gradual, incomplete recovery in all spheres, but no apparent residual visual defect
9 B. L.	47	Bitemporal defect—hemianoptic in left eye but irregular in right eye	Optic nerve atrophy and signs of pituitary tumor
10 S. C.	28	General constriction, most marked in 3 quadrants	Cerebral injury with shrapnel in occipital areas; in addition to hemianopsia, mild memory defect, slight aphasia, general intellectual slowness; defect in color vision demonstrated with pseudoisochromatic cards
11 M. M.	18	Homonymous hemianopsia; spontaneous recovery	Sudden onset of diplopia, followed by hemianopsia Cause congenital syphilis Complete remission during therapeutic course; mild exacerbation two months later

MacBeth illuminometer. The intensity was controlled by a variable resistance and neutral filters. Although this tended to alter the spectrum of the source, such a change was small and unimportant as far as this study was concerned. Precautions were taken to eliminate extraneous clues by presenting the target in a homogeneous, black, nonreflecting field within the dark room.

RESULTS

Perception of the Target.—In complete darkness, it was found that the patients could perceive the luminous target within defective (hemianoptic, quadranoptic or irregularly scotomatous) parts of their fields of vision. This perception was limited

4. Actually, the only sources of light, in an otherwise totally dark room, were those of the luminous target and the point of red light used as the fixation point.

to an awareness of light of an indefinite form and usually of a dim, whitish color. This ability was found to vary with the degree of darkness of the room, for when the background was illuminated with more than about 5 foot candles (measured at the background) a luminous target of $\log_{10} 7.2$ micromillilamberts within the defective field would disappear. When the illumination of the background was decreased or eliminated, the same luminous target would reappear.

The ability to see within the defective fields was found to fluctuate in all patients. Thus, even after enough time had been allowed for dark adaptation to occur and for the absolute visual threshold to be reached for all practical purposes, a continuously exposed target of threshold value might subjectively disappear, only to reappear spontaneously. There was no apparent regularity in this fluctuation of the absolute threshold. Compared with the nondefective fields, it was greater in degree and in frequency of occurrence. The quantification of this fluctuation in perceptive ability and of the thresholds of the defective fields will appear in a separate communication.

Not only was there an ability to see in defective fields under these conditions, but there were also indications of color perception. Two such indications were found when the defective areas were examined in complete darkness and with lights of sufficiently great intensities and long enough exposure. The first was the demonstration of different dark adaptation curves in response to lights of different wavelengths despite a subjective lack of appreciation of color. The second was the appreciation of color when the target intensity was raised well above the absolute threshold value and exposure was for periods longer than one minute.

The perception of form could not be demonstrated. For the most part, the target was perceived as a locus of light which imperceptibly faded into darkness and had no particular shape.

The illusion of movement sometimes occurred in both normal and defective fields when the target was exposed for 1/25 second. We cannot make any statement in regard to a difference in the normal and the abnormal in this respect. Actual movement of the target was appreciated in the frontoparallel plane but could not be demonstrated in the parasagittal plane (i. e., depth). Normal subjects also experienced difficulty in making judgments of movement of small luminous targets in the parasagittal plane when in a completely dark room.

Localization of the Target.—In addition to perceiving the target within the defective field, the patients could almost localize it correctly in space. Localization was tested in two ways—by having the patient place the tip of his index finger on the source of light and by having him estimate the direction and distance the target was removed from the fixation point. The patients could localize the source of light within their defective fields and make judgments of relative distance between the fixation point and the target within these defective fields. The judgments of relative distance in the frontoparallel plane were more accurate than judgments of relative depth in both the normal and the defective field. The occurrence of mislocalization was rare and will be discussed below.

Perception of Flicker.—The patients were able to distinguish between a steady and a flickering target within the defective field, in addition to perceiving and localizing luminous targets. This flicker perception was markedly affected by the previously described fluctuations in the visual threshold of the defective areas and

also by what were apparently persistent after-images, a topic which will be discussed in the presentation of the patients' subjective experiences.

All these results were found on numerous examinations of all the patients, in some cases over a period of more than one year.

Patients' Subjective Experiences.—To describe the subjective experience of seeing the target within the defective field, parts of the protocols of three cases will be cited.

CASE 1.—When the target subtended 2.5 degrees of retinal angle and was exposed for 1/25 second at threshold intensity at 90 degrees from the fixation point along the horizontal meridian of the defective field, A. F. described her experience as "a flash, a sort of grayish white . . . no definite shape . . . seems to move like a flash of lightning. . . . It's way out to my left . . . about 24 inches from the red light [fixation point] on the same level." When the target subtended 20 minutes of retinal angle and was exposed indefinitely at threshold intensity, the patient described her experience as, "You know how dawn is, just when it begins to get bright. . . . It's no definite color. . . . It's sort of dull gray . . . it has no shape." She could accurately point to the target which did not exhibit subjective movement. Great fluctuations in the subjective brightness of the target were experienced; at times it even became invisible. When the indefinitely exposed target was suddenly and silently extinguished, the subjective experience of light persisted for a time in the order of seconds. The longer the target was exposed or the brighter it was, the longer this "after-light" (after-image) persisted. On questioning, it was learned that this type of glare in the defective field had been experienced prior to our examination of this patient. She had such experiences "only at night . . . especially when I walk from dark to light or light to dark; then I notice brightness all over it [the defective side]. . . . It seems equal all over . . . as if some one puts on a light on my left side. . . . I don't get this in the daytime."

CASE 5.—The subjective visual experiences within the defective fields of E. G. were also interesting. When he was brought from a light to a dark room, he saw the "natural light of the room . . . a sort of glow." This was projected into his defective visual fields. It was present with the eyes opened or closed. After a few minutes, this sensation disappeared, and the room became completely dark for the patient. If now the luminous target was exposed continuously in the patient's defective field, he immediately reported the experience of light. After a few seconds there was a subjective change in this experience; the light became dimmer, and the glow (referred to above) began to appear, the light and the glow being superimposed. The glow was variously described as "a glow . . . a glimmer . . . a shimmer . . . sort of like the moon behind a cloud on a black night . . . not distinct. . . . It's sort of a yellowish-greenish-whitish cloud. . . . It makes you feel like the point of light is inside the shimmer." This glow became brighter as the intensity of the target increased, and it changed abruptly to a definite light with sharp borders when the target was moved into the nondefective field. Movement across the defective field would be appreciated correctly, but movement to or from the eye could not. In an attempt to define the nature of this glow, red and blue filters were placed in front of the luminous target. With the red filter the glow became "more greenish yellow," whereas with the blue filter it became "yellower and brighter." This and the observation that the glow disappeared if the patient was left in the dark suggest that the glow may have been a persistent after-image. The glow also showed subjective changes concomitant with other subjective visual phenomena experienced by this patient. One of his chief complaints was the occurrence of "something like snowfalls . . . bars of black . . . steps" on his right side, where he was aware that his vision was defective. On one occasion, when he was experiencing these visual sensations, he was placed in the dark room. The glow then appeared "as if I'm looking through a picket fence . . . it has black bars in it." On another occasion this patient was examined when he was using both eyes at once; no appreciable difference was noted between the phenomena observed in the binocular and the uniocular defective field.

CASE 7.—H. G. described his experience of the stationary luminous target within his defective fields as "something moving . . . sort of light . . . I can't really describe it. . . . It's like looking through those things [a kaleidoscope] you have as a kid; you looked in and

saw patterns, just patterns, no real shapes." For this patient, in addition to changes in intensity, movement of the objectively stationary target was experienced as the intensity of the target within the defective field was altered. He also experienced movement of the fixation point. These subjective movements did not have an obvious pattern in space or time. (Illusory movement of the sensation evoked by a stationary stimulus has also been found in tests of defective cutaneous modalities in many patients.) Fluctuation to the point of disappearance and reappearance of the target was common in this patient. Occasionally the target, which this man had experienced as light, suddenly changed to an experience of "something dark, darker than the darkness of the room," again suggesting that these phenomena have after-image-like qualities.

COMMENT

Before the significance of the data is discussed their validity must be considered. There is a possibility that the results we obtained with a luminous target in the blind field might be due to effects of entopic stray light and of retinal neural interaction. Bartley,[5] who did much of the original work on these factors, has an excellent discussion of them in his handbook. With respect to our work, the effects of these factors raise two considerations. The first is the manner of distribution of light on the retina when a single stimulus of threshold value is presented in an otherwise dark field. Fry and Cobb[6] proposed that this may be described by a gaussian curve, in which the abscissa represents distance on the retina and the ordinate the degree of illumination. This distribution also varied with the intensity and size of the stimulus, increasing as either of these parameters increased. In the particular case of our study, it is a question of whether the retinal distribution of a light stimulus subtending 2.5 degrees of retinal angle with an intensity of about $\log_{10}$ 5.5 micromillilamberts (the threshold of the defective area) is great enough to affect the retina of the normal visual half-field when such a stimulus is 90 degrees from the fovea along the horizontal meridian in the defective half-field of the same eye. The second consideration is whether this stimulus may initiate the visual sensory process by two other steps: first by exciting the apparently intact retina of the defective field (in our patients the lesions lay beyond the retina) and then by exciting that part of the retina associated with the unaffected visual field through retinal neural interaction.

From a review of our data, it would seem that entoptic stray light or retinal neural interaction is not the sole basis of the patient's ability to see and localize a glow in a perimetrically blind field under conditions of darkness. The following observations lead us to believe that the patient may actually be seeing in the apparently blind field.

1. The luminous target was accurately localized within the apparently blind area. This would seem to imply that the visual stimulus fell on the retina in the usual way and was correctly projected into space by the defective visual system. Were entoptic stray light or retinal neural interaction the important factor in initiating this visual experience through stimuli reaching the normal retina, it would be expected that the subjective experience would be projected away from the defective and into the normal part of the visual field. Obviously, this would result in mislocalization of the target to areas in the normal visual field. With

5. Bartley, S. H.: Vision: A Study of Its Basis; With an Historical Perspective, New York, D. Van Nostrand Company, 1941.

6. Fry, G. A., and Cobb, P. W.: New Method for Determining Blurredness of the Retinal Image, Tr. Am. Acad. Ophth. **40**:423-428, 1935.

stimuli of absolute threshold value, such mislocalization was found in only one instance. It occurred only with the right eye of A. F., and only with the target at 20 degrees of retinal angle along the 135 degree meridian (the upper defective quadrant). This mislocalization did not occur at 30 or 45 degrees of retinal angle in the same quadrant or at 20, 30 or 45 degrees of retinal angle in the lower defective quadrant of the same eye. No apparent reason for this mislocalization could be found. It was also observed that this mislocalization occurred only at or near the absolute threshold intensities. When, during the course of dark adaptation, the visual threshold was more than three times the absolute visual threshold, this mislocalization did not occur. On the other hand, when a stimulus subtending 2.5 degrees of retinal angle was of an intensity 1,000 or more times as great as the absolute visual threshold, was located in the defective field and was exposed to the fully dark-adapted eye for 1/25 second, every patient experienced a bright flash over the entire field of vision, normal and defective.

2. Localization was present and correct in the presence of a bilateral hemianopsia. H. G. had an almost complete bilateral homonymous anopia, but here, too, the target could be localized and thresholds and adaptation curves could be measured for various places in his visual fields. This would seem to be further evidence for ascribing a minimal role to entoptic stray light and retinal neural interaction in the explanation of our findings. It might be argued that in a left hemianopsia the light from a target in the left monocular visual field passes through the sclera of the left side of the eye, thereby stimulating the left side of the retina, and thus the non-diseased part of the visual system. If this were the case, it would be expected that the experience would be projected to the right visual field, unless the additional assumption is made that light reaching the retina "backward" is subjectively projected to the same side. However, the case of H. G. makes such reasoning unnecessary, for here both halves of the visual field were defective; yet targets in either half were correctly localized.

3. The luminous target could be perceived in the dark but not in light. When both halves of the visual field may be presumed to be defective, intraocular dispersion and retinal neural interaction could not account for the ability to see a target in the dark, yet not in the light. The case of R. F. is one in point. This patient, who had syphilis and a chiasmal space-occupying lesion, had apparently been completely blind for many years. When he was examined under ordinary room daylight, he could not tell whether it was light or dark. He was then placed in a dark room for 15 minutes, after which a brilliant light (General Electric 120 volt Reflector Flood) was turned on and off. Precautions were taken to eliminate auditory and thermal clues. Nevertheless, the patient could tell the difference between light and dark. He could not localize the light; it always seemed to be ahead of him.

4. The degree of darkness affected the visibility of the target within the blind field. Thus, if the target was unchanged but the room was faintly illuminated, thereby lessening the degree of darkness of the background, it was found that the target within the blind field became invisible. If now the background were made darker, the same, and unmoved, target reappeared. Within the normal field this target was visible with or without a dark background. Apparently, the two fields were functioning, but disparately.

5. The ability to see in the defective fields under conditions of darkness was parallel to the ability to adapt to darkness in the same regions. The results of

studies made on patients who recovered from a homonymous hemianopsia also indicate the minimal part played by dispersion and retinal neural interaction in the functional abilities of the defective visual parts. In the case of M. M., who recovered vision in the defective areas, the normal parts had normal dark adaptation curves and thresholds which did not change during the course of the illness or remission. However, the defective areas, which exhibited defective thresholds and adaptation curves during the illness, on the patient's recovery from the hemianopsia, as judged by perimetric measurements, had normal thresholds and adaptation curves. In the case of S. R., a similar parallel set of events was noted; as the hemianoptic defect cleared, the absolute threshold of the defective area, which had shown marked fluctuation, became like that of the normal areas. Since the perimetric and threshold changes occurred simultaneously and only in the defective fields, it is reasonable to assume that they are related and that the defective function may be attributed to the perimetrically blind areas.

6. There was ability to see the target in small scotomatous areas. This is another type of evidence indicating the small part, if any, played by entoptic stray light and retinal neural interaction in the phenomena under discussion. The study of A. M. showed that, although the scotomas were only about 5 to 9 degrees in width, there was a distinct difference (10 to 1,000 times) between the absolute visual thresholds of the scotoma and the immediately adjacent areas in either eye. Apparently, under the conditions of our work, the areas affected by entoptic stray light and retinal neural interaction were so small that regions 5 degrees from the center of the retinal image were not appreciably affected by these factors.

All these considerations suggest that the patient's ability to see in a perimetrically blind field under conditions of darkness is not due to retinal neural interaction and entoptic stray light. Nevertheless, the available evidence is not altogether conclusive. Indeed, recent work from our laboratory has shown that stray light or "neural interaction" may be a factor.

Battersby [7] examined our patients by the same method we did and obtained the same results. He then changed the method slightly by using a 2 degree luminous target projected through a tube. With this target he explored perimetrically blind fields under conditions of darkness. In examining the area occupied by the optic nerve, i. e., the blindspot, he found that most of the patients still saw the luminous glow when the target was within the area of the blindspot. This suggested that the ability to see the glow might be due to stray light. But such deduction is not warranted because one could not say whether it was actually the blindspot which was tested. Other observations made by Battersby [7] throw doubt on the theory of the stray light. Battersby found five patients with injury in the region of the parieto-occipital lobes who were unable to see the luminous target in the hemianoptic fields under conditions of darkness. This is in contradistinction to the results with the five he found, and with the many in our observation, who could see the glow. Since there were some who could and a few who could not see the target under the conditions stated, it would follow that stray light, which was present in each situation of testing, was not the factor which determines the ability to see in the apparently blind field.

7. Battersby, W. S.: Critical Flicker Frequency in Patients with Cerebral Lesions, J. Exper. Psychol, to be published.

It is obvious that we must leave open the question of interpretation of our data. At this time all we can say is that a luminous target can be seen and localized in a perimetrically blind area under the condition of darkness. Evidently, by modifying the usual conditions of testing, we were able to disprove the assumption that a perimetrically blind area is necessarily an area of complete loss of function. The necessary change in the condition of testing was examination of the defective area in darkness, instead of the ordinary room light of routine perimetry.

The results of our investigation lead us to postulate that some anopias are altered functional states rather than a total absence of function. This concept is not new, for Poppelreuter [8] expressed this view when he found that his patients were able to see targets exposed in the perimetrically blind areas under conditions of darkness. Moreover, experiments have shown that vision may be preserved to some extent after occipital lobectomies in animals. Smith [9] found that after extirpation of the striate cortex the cat cannot discriminate such simple patterns as vertical and horizontal bars under daylight illumination but is able to discriminate these patterns under low illumination. Klüver,[10] in carefully controlled studies, demonstrated that after removal of the occipital lobes, monkeys are able to see luminous flux, even though they lose pattern vision. In the light of Klüver's and Smith's investigations, two important questions are raised by our data: (*a*) whether the patient's ability to see in a blind portion of his field of vision under conditions of darkness is partly dependent on preservation of cerebral tissue remaining in the occipital lobe and (*b*), as a corollary, whether in patients who are unable to see there is total absence of the occipital lobe. In order to answer these questions, we must have exact anatomic studies, which thus far we lack. It was not the purpose of the present investigation to make anatomic correlations. Our chief goal was to show that anopias, determined by standard perimetry and illumination, do not necessarily imply complete absence of visual function in the affected regions.

SUMMARY

The visual fields of patients with lesions of the optic pathways were studied under conditions of daylight and darkness. Under ordinary illuminations, regions of blindness, scotomas or homonymous hemianopsias were found in the projected fields of vision. However, when these anopic regions were examined under conditions of almost total darkness with a faintly luminous target, the patient reported that he saw a minute source of light. He was able to see the luminous target at threshold values, differentiate changes in its intensity, perceive movement and localize its position, appreciate flicker and report after-images in the regions of the fields of vision. All these visual reactions were gross and showed much more fluctuation than those found in the normal portions of the fields of vision. The theory that retinal neural interaction and stray light are possible causes of the ability to see a luminous target in an apparently blind region of the field of vision under conditions of almost complete darkness was found to be inadequate.

8. Poppelreuter, W.: Die psychischen Schädigungen durch Kopfschuss im Kriege, Leipzig, Leopold Voss, 1917, vol. 1; 1918, vol. 2.

9. Smith, K. U.: Visual Discrimination in the Cat: V. The Postoperative Effects of Removal of the Striate Cortex upon Intensity Discrimination, J. Genet. Psychol. **51**:329-369, 1937.

10. Klüver, H.: Functional Significance of the Geniculo-Striate System, Biol. Symposia **7**:253-299, 1942.

Abstracts from Current Literature

Physiology and Biochemistry

EMOTIONAL HYPOTHERMIA IN RABBITS. R. GRANT, Am. J. Physiol. **160**:285 (Feb.) 1950.

It has long been known that rabbits become hypothermic on restraint, a condition which was first attributed to diminished heat production with immobilization and to increased heat loss due to exposure of greater skin areas, and later to anoxia and fear. Grant found that light restraint of rabbits in normal posture and without compression induced profound hypothermia by paradoxical activation of heat loss mechanisms. The effect was largely inhibited by exposure to cold and was completely inhibited by the injection of pyrogens. It was attributed to emotional factors.

ALPERS, Philadelphia.

PONTINE AND MEDULLARY REGULATION OF RESPIRATION IN THE CAT. C. G. BRECKENRIDGE and H. E. HOFF. Am. J. Physiol. **160**:385 (Feb.) 1950.

Breckenridge and Hoff found that apneusis in the cat is not permanent, nor does it supplant completely periodic respirations of a normal type. It diminishes and disappears with return of periodic respirations as deterioration progresses. Apneusis, or inspiratory spasm, fails to appear in the vagotomized animal when transections are made below the striae acusticae. Apneusis is considered to be an epiphenomenon arising from supramedullary centers and not intrinsically associated with the genesis of respiration.

ALPERS, Philadelphia.

INACTIVATION OF PARTIALLY PURIFIED POLIOMYELITIS VIRUS IN WATER BY CHLORINATION: III. EXPERIMENTS WITH NATURAL WATERS. S. G. LENSEN, M. RHIAN, M. R. STEBBINS and others, Am. J. Pub. Health **39**:1120 (Sept.) 1949.

Lensen and his associates previously reported an investigation on the inactivation by chorination of partially purified poliomyelitis virus (mouse-adapted Lansing strain) in distilled water. They now report further experiments in which representative samples of different natural waters were used instead of distilled water. The inactivation of partially purified poliomyelitis virus in natural waters was studied by chlorination of 100 cc. portions of water to which virus in natural waters was studied by chlorination of 100 cc. portions of water to which lake waters, two river waters and one lime-treated well water were used in the experiments. In samples of natural waters having a p_H range of 7.9 to 8.3 the virus was consistently inactivated within 10 minutes in the presence of 0.05 part per million of residual free chlorine at the end of this contact period. In many instances, but not always, the virus was inactivated by still smaller amounts of free residual chlorine. In experiments at a higher p_H range (10.0 to 11.25), 0.1 to 0.15 part per million of residual free chlorine was necessary to achieve the same results.

J. A. M. A.

Neuropathology

CYSTIC TUMOR OF THE THYMIC REGION AND MYASTHENIA GRAVIS: REPORT OF A CASE IN WHICH THE TUMOR WAS REMOVED. C. B. FULGHUM, Ann. Int. Med. **32**:327 (Feb.) 1950.

Fulghum reports a case of myasthenia gravis occurring in a white man who had rapid development of symptoms at the age of 56. Acute episodes had been precipitated by exertion, and he presented himself for study after an acute infection of the upper respiratory tract, which had aggravated his symptoms. The presence of a benign congenital cystic tumor of the thymic region was confirmed at operation, and the successful removal of this tumor was followed by prompt and sustained remission of the symptoms of myasthenia gravis.

ALPERS, Philadelphia.

CEREBELLAR DISORDERS IN LAMBS: A STUDY IN ANIMAL NEUROPATHOLOGY WITH SOME COMMENTS ON OVINE NEUROANATOMY. L. VAN BOGAERT, and J. R. M. INNES, Arch. Path. **50**:36 (July) 1950.

A disease of newborn lambs (of different breeds) with signs of incoordination and hypotonia was identified as occurring in Britain, where affected animals are known in local regions as "daft lambs." The primary lesions were restricted to the cerebellum and consisted of swelling, vacuolation and lysis of the Purkinje cells and, to a less extent, of the Golgi cells; glial reaction, initiated in the granular and Bergmann layers, was a consequent feature; corresponding neuronal and glial changes were present in many cases in the dentate and roof nuclei. The condition was regarded as a form of cortical cerebellar atrophy, and some evidence was given to show that it was inherited. An identical cerebellar condition was later established as occurring in Corriedale lambs in Canada; more data were available to indicate that the disease was inherited and due to a recessive gene.

The causal genesis is conjectural; it was suggested that it might be a metabolic, or toxic, disorder of cerebellar neurons occurring at a time in fetal development of the lamb when migration of Purkinje cells was nearly complete. Other "paralytic entities" have been confused clinically with that of "daft lambs," and cases of two such conditions are described: (*a*) angiomatosis with cerebellar atrophy and (*b*) a peculiar meningoencephalitis of the mesencephalon of uncertain etiologic origin.

WINKELMAN, Philadelphia.

PROGRESSIVE FIBRINOID DEGENERATION OF FIBRILLARY ASTROCYTES ASSOCIATED WITH MENTAL RETARDATION IN A HYDROCEPHALIC INFANT. W. S. ALEXANDER, Brain **72**:373, 1950.

Alexander describes the clinical and anatomic characteristics of a case of nonfamilial idiopathic cerebral sclerosis with fibrinoid degeneration of the fibrillary astrocytes. The patient, a 15 month old boy, was retarded in development. His skull measured 50 cm. in circumference, having increased 2.5 cm. during the month before admission. Neurological examination revealed only bilateral extensor responses to plantar stimulation. Necropsy revealed thrombosis of the cerebral venous sinuses. A greatly dilated cavum septi pellucidi bulged into the lateral ventricles, apparently compressing the foramens of Monro, with resulting moderate dilatation of the lateral ventricles. Histological studies of the liver showed foam cells, containing a doubly refractile lipid in the parenchyma.

In all sections of the central nervous system were large numbers of homogeneous fuchsinophilic bodies in the form of elongated rods, which were arranged radially around the walls of blood vessels in the white matter or perpendicularly to the surface of the brain in the subpial zone, but the cortex was spared. These bodies were similar in histological characteristics to the bodies seen in astrocytomas, especially the fibrillary type occurring in the third ventricle and the cerebellum in children. The astrocytes in the preparations showed varying degrees of degeneration. The authors state that "the morphology of the astrocytes in specific preparations provides definite evidence that these 'bodies' have resulted from degeneration of these cells and their processes."

FRANKEL, Philadelphia.

Psychiatry and Psychopathology

THREE TRIBUTARIES TO THE DEVELOPMENT OF AMBIVALENCE. E. BERGLER, Psychoanalyt. Quart. **17**:173 (April) 1948.

Bergler describes ambivalence as the presence of two contradictory feelings toward the same object at the same time. He describes three contributing factors to the mechanism: (1) the conflict between the autarchic defense mechanism and the regressive wish to be passively orally-anally penetrated; (2) a pseudoaggressive attempt to ward off passivity, and (3) utilization of pseudoaggression against oral-anal submission to narcissistic gratification. The common basis is a conflict between inner passive cravings and the fight against them by means of autarchic fantasies. The infantile sense of omnipotence of some infants is traumatically disrupted by the distorted perception of suckling as maternal aggression, as being passively pierced. Bowel training is later similarly misconstrued as being passively victimized. Against these misconceptions, aggressive and libidinous counterdevices are normally set in motion. When these countermeasures do not suffice, ambivalence develops, especially in children who regress

to the anal stage. Ambivalence is the outward manifestation of a desperate unconscious struggle between the wish to be orally and anally penetrated and an anxious denial of this dangerous wish by pretending aggressively that autarchy is preserved. WERMUTH, Philadelphia.

THE CONCURRENT ANALYSIS OF MARRIED COUPLES. B. MITTELMANN, Psychoanalyt. Quart. **17**:182 (April) 1948.

Mittelman believes that the treatment of married couples by the same psychoanalyst makes more concrete both the realities and the neurotic interactions of the mates. Current reactions of dependency, guilt, hostility, anxiety and superiority are revealed in a clearer light, and at times one of the mates gives information about crucial trends in the other. Transference reactions include concern about whether the analyst favors the other, whether he values the mate as highly or as poorly as the patient, fear of divorce or separation and the defense of unattainable marital ideals. Increased tension may develop if the mates (mis)quote the analyst to each other during new situations of stress or if one of the mates has a negative therapeutic reaction or stops treatment. According to Mittelmann, simultaneous treatment of married couples was successful in 11 of 12 instances, including two which ended in divorces satisfactory to both parties. In four of the 12 cases both mates were analyzed. In eight, one mate was analyzed; the other received briefer psychotherapy.

WERMUTH, Philadelphia.

EFFECTS OF SHOCK TREATMENT ON THE EGO. J. FROSCH and D. IMPASTATO, Psychoanalyt. Quart. **17**:226 (April) 1948.

Frosch and Impastato believe that shock treatment is an experience which produces alterations in the somatopsychic homeostasis leading to a disruption of the hitherto existing mechanisms that tend to maintain this homeostasis. In its attempts to reestablish the hitherto existing equilibrium, the ego may be successful, partially successful or unsuccessful, with the production of various clinical syndromes. The ego may defensively regress to more primitive, narcissistic levels. This step brings with it more archaic defensive mechanisms, in the attempt of the ego to hold on to some degree of reality. This state may be only temporary, and after a time it is possible that the ego may muster its forces and reestablish its previous or, perhaps even a better, adaptive, defensive apparatus. All these maneuvers produce varying kinds of clinical reactions.

WERMUTH, Philadelphia.

ANAL SENSATIONS AND FEELINGS OF PERSECUTION. J. A. ARLOW, Psychoanalyt. Quart. **18**:79 (Jan.) 1949.

Arlow cites excerpts from the analysis of a nonpsychotic patient who had fantasies of persecution which he believes confirm the observations of other investigators that the persecutor may unconsciously be equated with the subject's feces in the rectum. Tormenting anal sensations are projected to the homosexual object in the external world and transformed into feelings of persecution. The correlation of constipation and feelings of persecution with the analysis of the transference relationship led the author to believe that in this instance there occurred an unconscious form of anal masturbation in which the fecal mass aroused sensations in the subject's rectum in response to masochistic feminine fantasies. The fecal mass also represented the penis of the homosexual object and, in a fantasy of pregnancy, the fetus. Arlow points out that the analyst should be alert to detect references or associations to anal sensations whenever patients in analysis are preoccupied with fantasies of persecution or assault.

WERMUTH, Philadelphia.

DREAMS FOLLOWING INTERCOURSE. V. W. EISENSTEIN, Psychoanalyt. Quart. **18**:154 (April) 1949.

Eisenstein quotes Groddeck's statement: "It is not true that sexual intercourse is the culmination of erotic life. People are really bored with it." The author belives this statement to be correct for psychoneurotic persons who suffer from overt or cryptic sexual maladjustments. He reports numerous examples of postcoital dreams. These dreams reveal the immediate factors

responsible for lack of sexual satisfaction and for the resultant moods of irritability and depression. The considerable emotional significance of such dreams is a factor which may be utilized in the interest of psychotherapy. As neurotic conflicts are resolved, alterations in unconscious attitudes may be advantageously observed and the clinical progress evaluated in the dream reactions to a standard heterosexual stimulus.

WERMUTH, Philadelphia.

Diseases of the Brain

ABSCESS OF THE FRONTAL LOBE SECONDARY TO ETHMOIDITIS. JOSEPH H. KLER, Arch. Otolaryng. **49**:125 (Feb.) 1949.

Abscess of the brain is an extremely rare complication of ethmoiditis. In view of the common occurrence of ethmoiditis, the rarity of this complication can best be explained by the intrinsic structure of the ethmoid sinuses, together with the nature of their blood supply. The anatomic arrangement of the ethmoid cells favors the isolation of low grade infection. There is a rich blood supply with many anastomoses, and the lymphatic drainage is chiefly away from the intracranial region. The extension of infection from the ethmoid cells is either by contiguity or by thrombophlebitis of one of the veins communicating with the dura.

Kler reports on three patients with abscess of the frontal lobe of ethmoidal origin. The first patient was a 5 year old child in whom an acute abscess of the frontal lobe developed after acute ethmoiditis. The other two patients were adults in whom chronic abscesses of the frontal lobe followed chronic ethmoiditis. Because chronic encapsulated abscess of the brain in the presence of low grade infection of the ethmoid sinuses is difficult to diagnose, the condition may progress to a critical stage before the patient seeks medical attention. This was true in both the second and the third case cited.

Complications of acute ethmoiditis occur more frequently and are more easily diagnosed than those of chronic infection. Chronic abscesses of the brain secondary to ethmoiditis give few signs and symptoms at first, except for papilledema. Electroencephalography has been found to be an invaluable aid in the diagnosis of such cases.

RYAN, Philadelphia.

FUNCTIONAL AND ANATOMIC RELATION OF SPHENOPALATINE GANGLION TO THE AUTONOMIC NERVOUS SYSTEM. DAVID HIGBEE, Arch. Otolaryng. **50**:45 (July) 1949.

Higbee believes that the sphenopalatine ganglion should no longer be associated with the sensory nervous system but should be considered a part of the parasympathetic nervous system. The sphenopalatine ganglion has been of clinical interest for some time because of its association with pain. The therapeutic procedures of cocainization and injection of the ganglion to relieve "sphenopalatine neuralgia" have no true anatomic basis. The sphenopalatine ganglion is associated with the parasympathetic nervous system, and secretory and vasodilator impulses are relayed from the superior salivary nucleus to the lacrimal gland and mucosa of the upper respiratory tract. Fibers from the fifth nerve merely pass through the sphenopalatine ganglion and have no functional relation to the ganglion.

Observations following paralysis of the sympathetic nervous system, section of the fifth sensory root and administration of atropine led to the following conclusions: 1. Vasoconstriction is the dominant effect of stimulation of the sympathetic nerve fibers. 2. Sensory innervation of the nasal mucosa is from the fifth cranial nerve. 3. Vasodilatation and secretory regulation of the nasal mucosa through the fibers from the sphenopalatine ganglion are the functions of the parasympathetic nervous system.

RYAN, Philadelphia.

RECURRING MASTOIDITIS, MENINGITIS AND ABSCESS OF THE RIGHT TEMPOROSPHENOID LOBE. BENJAMIN H. SHUSTER and MEYER A. MARKS, Arch. Otolaryng. **50**:462 (Oct.) 1949.

Shuster and Marks report the case of a 12 year old boy with a history of recurring mastoiditis who was brought to the hospital in a stuporous condition. Dilatation of the homolateral pupil and a positive Macewen sign pointed to a diagnosis of abscess of the right temporosphenoidal lobe. After surgical drainage of the abscess, a tube was left in place for a time, but meningeal signs developed later. Further drainage became necessary, and recovery ensued. The authors stress that use of penicillin should not be discontinued too soon nor should a drainage tube be removed too early.

RYAN, Philadelphia.

BIRTH INJURY, FOCAL EPILEPSY AND CORTICAL EXCISION: CASE REPORT. W. PENFIELD and S. LIVINGSTON, Pediatrics **4**:157 (Aug.) 1949.

Penfield and Livingston report a case of brain injury at birth in a boy now aged 8 years. There was no history of epilepsy or convulsions in other members of the family. He vomited several times two days after birth and had two generalized convulsions. Vomiting and three more convulsions occurred within the subsequent two days. He was given vitamin K and treated symptomatically. He held up his head at 3 weeks and sat alone at 4 months, and his mental development seemed to be normal until he reached 6 months of age. Recurring cerebral seizures began at 5 months, and soon thereafter there was decided deterioration. He could not hold up his head and became completely apathetic. He was treated with phenobarbital, bromides and diphenylhydantoin sodium, with little benefit. Roentgenographic examination of the skull showed that the right cranial chamber was smaller than the left. Preoperative encephalography gave evidence of a focal epileptogenic lesion in the right hemisphere in the vicinity of standard head position C6. At the age of 12 months the patient was subjected to a large osteoplastic craniotomy on the right side, with removal of narrow, tough gyri bordering a fluid-filled space adjacent to and within the frontal lobe. The simple excision of these half-destroyed gyri resulted in cessation of seizures. It terminated the deterioration of the infant and permitted resumption of more or less normal development. The patient has now a chronologic age of 8 years 4 months, a mental age of 6 years 2 months and an intelligence quotient of 69 per cent. Birth trauma may produce a local cerebral lesion which is relatively unimportant until it ripens into the epileptogenic focus, from the generalized influence of which intellectual and behavioral deterioration may sometimes result. This ripening process may require six months to twenty years.

J. A. M. A.

CONGENITAL BASAL CEREBRAL ANEURYSM AND POLYCYSTIC KIDNEY. W. SUTER, Schweiz. med. Wchnschr. **79**:471 (May 28) 1949.

Suter reports the simultaneous occurrence of congenital aneurysm of basal cerebral arteries and polycystic kidney in 10 men and five women between the ages of 24 and 56, as mentioned in the literature. He reports two cases of his own—one of a woman aged 56 and one of a man aged 36. There seems to be a slight preponderance in the male sex. Both conditions are malformations. Multiple malformations in the same person are considered characteristic of all congenital anomalies. Twenty-seven cases of congenital aneurysm of basal cerebral arteries were observed in a series of 5,960 necropsies performed at the pathological institute of the cantonal hospital in St. Gallen, Switzerland, from 1941 to 1947. In two instances in which a congenital aneurysm of the cerebral vessels was demonstrated, there was associated polycystic kidney. In both the author's cases death resulted from spontaneous subarachnoid hemorrhage due to rupture of a congenital aneurysm of the anterior communicating artery. Bilateral polycystic kidney was observed in both cases. Both malformations may be placed within the nosological frame of Bard's syndrome of idiopathic dilatations, or, according to Snapper and Formijne, they may be interpreted as simultaneous failures in junction of two systems growing toward one another. The prognosis is unfavorable for congenital aneurysm of basal cerebral arteries associated with polycystic kidney because of the possibility of a precocious rupture due to nephrogenic hypertension.

J. A. M. A.

Diseases of the Spinal Cord

HEREDOFAMILIAL CEREBELLAR ATAXIA WITH SPASTIC PARALYSIS AND SPINAL MUSCULAR ATROPHY: REPORT OF TWO CASES OF AN UNUSUAL SYNDROME. EDWIN DENNIS KILBOURNE, J. Nerv. & Ment. Dis. **109**:409 (May) 1949.

Kilbourne reports the cases of two siblings with a hereditary familial disease of the nervous system regarded as a variant of the Charcot-Marie-Tooth and Friedreich types of disorder. Both patients had a relatively normal developmental history until the age of 13, except that the first, a man aged 25, had had one febrile convulsion at the age of 15 months. At the age of 5 years he spoke rapidly and explosively and tended to walk on his toes. This speech difficulty increased at the age of 13, when his hands became clumsy. His legs began to be spastic and his extremities weak at 17 years of age. Fasciculations of the legs developed at the age

of 22. Examination disclosed pronounced lordosis; spastic-ataxic gait; garbled, explosive, nasal speech; facial grimacing; atrophic extremities; fasciculations of the arms, chest and legs; incoordination of the arms and legs; increased resistance to passive stretch in both arms and legs, and pes cavus. Reflexes and sensory modalities were intact.

In the other patient, a single woman aged 29, progressive speech difficulty, ataxia and weakness of the legs appeared at the age of 13 years. As her disability increased, her personality became distorted, so that she was suspicious, irritable and subject to frequent tantrums of rage. Examination revealed poor physical development, with symmetrically wasted extremities. The gait was spastic-ataxic on a wide base, with falling to the right with eyes open or closed. The speech was nasal, explosive, slurred and accompanied with grimacing. The muscles of the trunk and extremities were atrophic, weak and incoordinate in rapid alternating movements. Fasciculations and increased resistance to passive stretch were evident in the left arm. Sensory modalities were normal. The reflexes were increased, and there was an inconstant Babinski sign on the right.

Laboratory studies revealed nothing abnormal. Two paternal uncles had a similar condition. The two patients whose cases are reported resemble the father, while two other siblings, who resembled the mother, were not affected.

FARMER, Philadelphia.

MUMPS COMPLICATED BY PRECEDING MYELITIS: REPORT OF FATAL CASE. A. C. SILVERMAN, New England J. Med. **241**:262 (Aug. 18) 1949.

Silverman reports a fatal case of mumps myelitis in a physician aged 37. There had recently been a number of cases of mumps in the patient's area, and he had seen two patients with meningoencephalitis. Symptoms and signs of myelitis preceded swelling of the parotid gland by three days. Death ensued within eight days and was caused by pulmonary involvement consistent with virus disease, but whether it was caused by the primary virus is problematic. Necropsy revealed focal lymphocytic infiltration of the parotid gland with preservation of the general acinar cell structure and pyknosis of some nuclei. Sections from the cerebral cortex revealed some demyelination and lymphocytic infiltration. Sections from the anterior horns of the cervical portion of the cord showed appreciable perineuronal edema. Both lungs were heavier than normal, deep purple and nonaerated. Sections from the lungs showed exudate with polymorphonuclear cells within the bronchial lumen, sloughing of bronchial epithelium and infiltration of the submucosa. The alveoli were relatively free of exudate, although scattered lymphocytes, monocytes and plasma cells were seen. The interstitial tissue also showed mild infiltration with these cells. In the literature on mumps there is no description of the disease in the lung, as in the author's case. The virus studies supplied only negative results, but failure to isolate mumps virus from the postmortem tissues can have no bearing on the pathological diagnosis. The new complement fixation antigens, the virus-bound (V) antigen and the soluble (S) antigen were not as yet available. Since then, the use of both these antigens has made possible the early diagnosis of manifestations of mumps as meningoencephalitis in the absence of parotitis.

J. A. M. A.

ACUTE ANTERIOR POLIOMYELITIS IN 1947 WITH SPECIAL REFERENCE TO LONDON. ALAN DALEY, Proc. Roy. Soc. Med. **41**:52 (Jan.) 1948.

In 1947 England had the largest epidemic of poliomyelitis in its history. Assuming notification of cases to be a rough guide to incidence, the most interesting features in recent years in England and North America are (1) a shift toward the older age groups and (2) an increase in the cases of brain stem involvement. There is evidence that more persons now reach adolescence or adulthood without acquiring immunity because of better standards of sanitation. This is suggested by the minimal incidence of poliomyelitis among adults in Japan and its frequent occurrence in the American occupation forces, and the predominance among children under 5 years of age in endemic areas, such as Malta and Mauritius. In St. Helena, however, where the disease was previously unknown, the highest incidence was in the age group of 10 to 25 years. The adult is more likely to have the bulbar type.

The human patient or carrier provides the two important means of spread: droplets from the nasopharynx and excreta.

A reservoir of poliomyelitis has always existed in London, with the seasonal peak about mid-September, most cases occurring between July and the end of November. Up to Oct. 25, 1947, there were 908 cases reported in London, more than in the entire decade of 1937 to 1946. Whereas in the preceding decade 78 per cent of the patients were under 15 years of age, in 1947 this figure was 64 per cent. Among patients under 15 years of age there was an excess of males of 1.23:1. Comparison of the incidence for each metropolitan borough showed that boroughs with a significantly higher rate were surrounded by boroughs in which the incidence was close to the average for London as a whole and which were clearly "isolated areas for high incidence." Several possible factors to account for this difference are discussed and discarded as without proof: (*a*) more complete notification, or overnotification; (*b*) social conditions; (*c*) differences in immunity level, and (*d*) differences in method of control.

Age Incidence.—In the age group of less than 5 years, there was a drop from 55 per cent, in 1921-1923, to 27.4 per cent, in 1947, the latter despite a reversal in the population trend, suggesting either a change in the virus to which older age groups are susceptible or increasing immunity in infants.

Overcrowding.—The risk of multiple cases in a family is 3 per cent, indicating that contact is not important, that the rest of the family is immune or that, although the whole household is infected, only one clinical case develops. There is statistical evidence that true paralytic poliomyelitis is less common in overcrowded households.

The histories of contact and exposure of 391 hospitalized patients offered little or nothing of value.

General Epidemiological Considerations.—"Very few lessons have emerged from our analysis. We do not know why the disease was so much more prevalent in England in 1947 than ever before. . . . Authentic cases are reported of second attacks." There is a suggestion that a larger proportion of the population had failed to be immunized in infancy, possibly because of improved sanitation.

Of 391 cases analyzed, confirmed hospital cases, 34.8 per cent were of the abortive and 8.5 per cent of the bulbar type. The case mortality was 5.1 per cent; the incidence of complete recovery was 54.2 per cent. In 6 per cent of the cases a respirator had to be used at one time or another. It is estimated that 25 per cent of patients will have a limited working capacity and that the working capacity of 5 per cent of the 391 patients will be almost nil.

BERRY, Bethesda, Md.

SPINAL COMPLICATIONS FOLLOWING SPINAL ANESTHESIA. M. STREIFLER, Confinia neurol. **10**:96, 1949.

Streifler reports six cases of spinal complications following spinal anesthesia. A brief summary of the cases follows.

CASE 1.—A woman aged 37 had had a myomectomy, with intrathecal injections of 200 mg. of procaine hydrochloride. Four days after operation she complained of clumsiness in her left leg and a sensation of "needles" in the back of the left foot. Examination showed foot drop, weakness of flexion and extension of the knee and diminished ankle jerk, all on the left side, and a sensory deficit to pain and touch involving the fourth and fifth lumbar and first sacral segments. Satisfactory recovery occurred within a few weeks.

CASE 2.—A woman aged 53 had had a hysterectomy, with intrathecal injection of 75 mg. of procaine hydrochloride. On the first postoperative day she complained of formication and of clumsiness from the left knee downward. Examination showed foot drop and toe drop and a diminished ankle jerk on the left side, with reduced sensation over the fifth lumbar and first sacral dermatomes on the left side. There was considerable improvement one month later.

CASE 3.—A girl aged 16 had had an appendectomy under spinal anesthesia, the quality and quantity of the anesthetic being undetermined. At the time of introduction of the spinal needle she felt violent pains along the right leg. After recovering from the anesthesia, she was unable to move the right leg, which was again painful. She had had no relief six months later, when examination showed complete paralysis of the muscles of the right calf and foot, weakness of flexion and extension of the right knee, reduction of sensation over the fourth and fifth lumbar and first and second sacral segments on the right and trophic ulcers in the hyposensitive areas. There was recovery of some function, aided by arthrodesis.

CASE 4.—A woman aged 42, a known diabetic, had had a nephrectomy, with anesthesia obtained by intrathecal injection of 150 mg. of procaine hydrochloride. One month later there was observed a foot drop and toe drop, absence of the abdominal reflexes and the knee and ankle jerks and reduction of sensation over the fifth lumbar and first sacral segments, all on the right side. There was some recovery of motor function.

CASE 5.—A man aged 41, with thromboangiitits obliterans had had a bilateral lumbar sympathectomy, with intrathecal injection of 200 mg. of procaine hydrochloride. Ten days after operation he was unable to pass urine for two days and then experienced violent pains and weakness in both legs. Examination showed reduction of sensation from the tenth thoracic level down, with sparing of the sacral segments. Two months later weakness of both legs had developed.

CASE 6.—A man aged 61 had had a paravertebral injection of a "procaine derivative" for pain in the right leg and hip, with immediate development of paralysis of the legs and loss of sensation up to the chest. He made a remarkable improvement almost to complete recovery of function.

FOLEY, Boston.

Peripheral and Cranial Nerves

HERPES ZOSTER OTICUS ("RAMSAY HUNT SYNDROME"). LEIGHTON JOHNSON and BERNARD ZONDERMAN. Arch. Otolaryng. **48**:1 (July) 1948.

Johnson and Zonderman call attention to the work of Tschiassny, in 1946, challenging the tenets of Ramsay Hunt and emphasize that the term "Hunt's syndrome" or "geniculate zoster" should be reserved for those cases in which the lesion can be demonstrated in the geniculate ganglion, either by histopathological study or by topognostic analysis.

An unusual case of herpes zoster oticus with facial paralysis, Ménière's symptom complex and a high degree of lymphocytosis of the cerebrospinal fluid is recorded. Many observers have stressed that the spinal fluid is frequently involved in herpes zoster, and when lumbar punctures are done routinely in cases of herpes zoster more instances of abnormal cerebrospinal fluid will undoubtedly be reported.

RYAN, Philadelphia.

AUDITORY NERVE IN MULTIPLE SCLEROSIS. HANS VON LEDEN and BAYARD T. HORTON, Arch. Otolaryng. **48**:51 (July) 1948.

Though a number of isolated instances of deafness occurring in cases of multiple sclerosis have been reported in the literature, very little attention has been given to a study of involvement of the auditory nerve in this disease. Microscopic examinations have confirmed the belief that the auditory nerve is involved in multiple sclerosis.

Von Leden and Horton studied the hearing of 92 patients with a condition diagnosed as multiple sclerosis. All these patients had the classic symptoms and signs of the disease, were under 50 years of age and showed no indication of previous disease of the middle ear. The examinations of the auditory nerve were carried out under basal conditions in a soundproof room with an especially calibrated audiometer. Fifty-three patients (57 per cent) had normal hearing; 39 (43 per cent) showed a measurable degree of deafness. Of these, 6 had slight loss of hearing but could still understand normal conversation; 24 had slight to moderate loss of hearing for higher frequencies in one or both ears, and the other 9 had moderate to severe unilateral field defects for higher frequencies which were compensated by the ability of the unaffected ear to hear.

No relation was noted between the severity of the disease and the decrease in hearing. Nystagmus and vertigo were investigated to determine the vestibular involvement. Eighteen cases of true rotatory nystagmus and eight cases of dissociated nystagmus, considered a pathognomonic sign of multiple sclerosis, were found, demonstrating the destructive effect of the disease on the associated nuclei of the auditory nerve, as well as on the nerve itself.

RYAN, Philadelphia.

MÉNIÈRE'S SYMPTOM COMPLEX: ITS RELATION TO CHEMISTRY; AN ETIOLOGIC STUDY. GRANT SELFRIDGE. Arch. Otolaryng. **49**:1 (Jan.) 1949.

An extensive review of the pertinent literature is given by Selfridge in support of his statement that Ménière's disease is not caused by any one process but is related to all the factors involved in growth, such as endocrine products, electrolytes, amino acids and vitamins. As a result of these studies, the treatments advocated for Ménière's disease, in addition to surgical procedures, are (*a*) those related to metabolism of salt and water, (*b*) those related to metabolism of potassium, (*c*) those using certain vitamins and (*d*) those related to the use of histamine. Surgical section of the labyrinthine branch of the eighth nerve is done less frequently now, since the most favorable results seem to have followed the use of several of the vitamins, especially thiamine, nicotinic acid and a member of the choline group. The close alliance between the chemical structures of the endocrine substances and those of the vitamins indicates that Ménière's disease is related to the body chemistry and to disturbances of nutrition.

RYAN, Philadelphia.

MÉNIÈRE'S SYNDROME; OBSERVATIONS ON VITAMIN DEFICIENCY AS THE CAUSATIVE FACTOR: I. THE VESTIBULAR DISTURBANCE. MILES ATKINSON, Arch. Otolaryng. **49**:141 (Feb.) 1949.

Eighty-seven patients with classic Ménière's syndrome were investigated from the standpoint of deficiency in the three major components of the vitamin B complex (niacin [used here to include nicotinic acid and nicotinamide], riboflavin and thiamine) over a period of twenty-one months. These patients showed the full-fledged triad of acute paroxysmal vertigo, deafness and tinnitus, predominantly or entirely unilateral. Only the acute phase was dealt with in this study. These cases were divided into three groups depending on their response to intradermal injection of histamine.

Subjects with Ménière's disease experience rotational and positional vertigo, and observations showed that these two distinct types are related to different specific vitamin deficiencies. Those who experience rotational vertigo alone show signs of nicotinic acid deficiency in the tongue, give small response to intradermal injection of histamine and can be relieved of their attacks with nicotinic acid. Patients who experience positional vertigo alone show signs of riboflavin deficiency in the tongue, the eyes and the skin, give a large response to histamine injected intradermally and can be relieved of their attacks with riboflavin. The majority of the patients fall into a third group. In this group the patients experience both kinds of vertigo, show signs of a deficiency in both fractions, give an intermediate response to intradermal injection of histamine and can be relieved of their attacks only if both fractions are administered.

It was found that the routine addition of thiamine potentiated the action of the other fractions used in this series of cases and relieved the symptoms of fatigue, irritability and palpitation, commonly occurring in patients with Ménière's syndrome.

The doses administered were arrived at after considerable experience and investigation. It was found advisable to begin with small doses given parenterally and orally and gradually to increase the doses until the acute symptoms of the attack are controlled. Then the patient can be maintained on oral administration for such time as is deemed necessary to prevent recurrences of the symptoms.

RYAN, Philadelphia.

Treatment, Neurosurgery

THE SURGICAL TREATMENT OF SPONTANEOUS AND TRAUMATIC INTRACEREBRAL HEMORRHAGE. F. C. GRANT and G. M. AUSTIN, Am. J. M. Sc. **219**:237 (March) 1950.

Grant and Austin report 14 verified cases of cerebral hemorrhage, five of traumatic and nine of spontaneous type, in all of which operation was performed. The age incidence seems to be unimportant, except that it appears to be higher for cases of spontaneous hemorrhage than for those of traumatic hemorrhage. Sudden loss of consciousness occurred in 10 cases and was regarded as an important diagnostic sign. Advancing stupor is important. Hemiparesis or hemiplegia was present in 11 cases; in three others there was no hemiplegia. In four

cases there was some degree of papilledema. Spinal fluid pressure was measured in 11 cases, in six of which it was increased. The spinal fluid was pink or bloody in six cases and was slightly xanthochromic in two cases. Diagnosis is difficult. Of the present series, a diagnosis of brain tumor was made in four, of subdural hematoma in four, of extradural hemorrhage in three, of cerebral abscess in one and of cerebral hemorrhage in two.

Neither the time interval after onset of symptoms nor the type of operation affected the operative results. In seven cases the blood was evacuated through a burr hole, and in six cases an osteoplastic craniotomy was performed. In two of five cases of traumatic type (40 per cent) the condition was fatal, as it was in two of nine cases (22 per cent) of non-traumatic type. The over-all mortality for the 14 cases was 28.6 per cent.

ALPERS, Philadelphia.

BACTERIAL MENINGITIS: RESULTS OF TREATMENT IN SEVENTEEN CASES WITH A NEW SULFONAMIDE (GANTRISIN®). P. S. RHOADS, F. A. SVEC and J H. ROHR, Arch. Int. Med. **85**:259 (Feb.) 1950.

Ten patients with meningococcic meningitis were treated with gantrisin,® a new sulfonamide with the formula 3,4-dimethyl-5-sulfanilamide-isoxazole, which was used as the sole bacteriostatic agent. All recovered without complications resulting from the disease or the treatment.

Two patients with meningococcic meningitis, three with pneumococcic meningitis and two with hemophilus influenzae meningitis were treated with gantrisin® and one of the antibiotics. One of these patients, shown at autopsy to have had pneumococcic endocarditis, died. All the others recovered.

Gantrisin® was administered orally, intramuscularly and intravenously, with no untoward effects. Several patients who had albuminuria and microscopic hematuria at the start of treatment with gantrisin® were given the drug in full doses without adjuvant alkali therapy; the conditions cleared up under treatment.

ALPERS, Philadelphia.

Society Transactions

CHICAGO NEUROLOGICAL SOCIETY

Alex J. Arieff, M.D., President, in the Chair

Regular Meeting, Dec. 13, 1949

Unselected Cases of Spina Bifida in the Newborn Treated Surgically. Dr. William R. Chambers, South Bend, Ind.

The policy of operating for severe myelocele and meningomyelocele within the first few days to weeks of life was adopted, on the theory that waiting would only allow time for further traction on the upward migrating cord.

Ten consecutive cases were accepted without selection. In eight cases a part of the cord was incorporated in the sac—true myelomeningocele; in two there was preoperative evidence of hydrocephalus, which failed to progress after operation, and in one, in which neither the foot nor the leg was moved, the use of both was regained. Seven infants appear destined for a normal or near normal existence; in 2 hydrocephalus developed, and 1 died of an intercurrent infection. The steps of the technic were described.

DISCUSSION

Dr. Harold C. Voris: Dr. Chambers is to be congratulated on his courageous attack in unselected cases of myelomeningocele. I agree that, with the precautions which he has so carefully exercised, it is possible to operate on the newborn infant with unepithelized myelomeningocele without serious risk of infection or fatality. I am not sure, however, that it is the expedient thing to do. I must confess that my own policy of waiting at least a month before operation is one of giving the family, and sometimes the referring physician, time to orient and adjust themselves to the serious neurologic defect. If Dr. Chambers' astonishingly favorable early results are borne out by time, he will have demonstrated that early operation has value. It seems to me that as these children grow there may still be difficulty with adhesions of the lower end of the spinal cord to the overlying tissue and that, with increasing traction on the cord and nerve roots, late neurologic signs in the lower extremities, such as are common in various types of spina bifida occulta, may become apparent. I hope that will not be the case. I am interested in a comment on the matter of determination of normal function of the sphincter in the newborn or the very young infant.

Dr. Milton Tinsley: In our selection of patients for surgical treatment, my associates and I usually place a great deal of emphasis on the absence of neurologic signs, the absence of paralysis being an indication of operability in cases of this defect. In the case of meningomyelocele it is the presence of paralysis of the lower extremity or the sphincter which indicates the presence of the cauda equina or the spinal cord in the sac and leads to a poor prognosis. Dr. Chambers spoke of the spinal cord or cauda equina being incorporated in the sac without any evidence of paralysis in 5 or 6 cases, an exceptional series. I should like to have him explain the absence of paralysis in his cases.

Dr. George Hassin: Certain pathologic features of spina bifida may explain why one cannot expect cure of this morbid condition. Spina bifida is a maldevelopment in which not only some parts of the vertebrae are missing (which would not be so serious) but also the adjacent dura mater and, what is worse, the spinal roots and even the spinal ganglia are more or less affected. Such a combined destruction prevents the escape of the cerebrospinal fluid, causing its accumulation in the subarachnoid space and leading to the formation of a protruding bag filled with the fluid. Depending on the location, the bag contains, in addition, spinal roots (meningocele) or spinal roots with some segments of the spinal cord (myelomeningocele) attached to them. In myelomeningocele, the spinal cord is damaged and is therefore not accessible to treatment, while in meningocele surgical treatment may give only temporary relief, as the perineurial root spaces through which the spinal fluid escapes are destroyed.

For these reasons, the good results demonstrated by Dr. Chambers in the infants he operated on cannot be expected to be permanent.

DR. WILLIAM R. CHAMBERS: The problem of determining whether a sphincter is intact is a difficult one. I admit that the tests which are available to us in South Bend may be rather inadequate. We do try to determine, as best we can, without the laboratory facilities available in a larger community, the intactness of a sphincter; we look at the rectal sphincter, and see whether it will contract on stimulation of the surrounding skin; we hold the baby up and make sure that the sphincter is not patulous; we find out what we can from the nurses about the stools, whether they run out or seem to be controlled, and we hold the baby up and see whether the urine flows when the baby is held in an erect position. That is about all we have to go by in South Bend. If we had more laboratory facilities, we might do better. Dr. Tinsley, I cannot answer your question as to why there are no more neurologic deficits with elements in the sac; I can only report to you what we saw at operation—neural elements tightly adherent to the sac wall, and in other cases the spinal cord making a part of that wall and merging with it. However, these babies moved both lower extremities and had, as nearly as we could determine, an intact sphincter. In 1 case, as described in the literature, there was a soft, meaty, yellowish granulation on the surface of the sac, otherwise described as an undeveloped portion of the nervous system. That is about as far as we have gone in our short experience. I defer to Dr. Hassin's greater knowledge of, and experience in, neurology. Whether these babies will finally reach a satisfactory condition is, I believe, something I shall have to report on later. The present results have given us only an indication that a therapeutic result better than we could have expected might be possible. If this is true, and these babies continue to do well, I shall give you a further report.

Topectomy: Its Application in the Relief of Pain. DR. MILTON TINSLEY.

Topectomy was performed in 6 cases of intractable pain, including facial pain, the pain of inoperable carcinoma and, in 1 instance, postherpetic neuralgia. In all but 1 case the relief was excellent, the longest effective period to date being five months. After the topectomy the desire for narcotics was lost.

I decided to employ topectomy because of the poor results following radical bilateral or unilateral lobotomy. The mental deterioration, the early death of the patient after lobotomy and the early return of pain led me to give up its use in the painful state. Following topectomy, the reaction to pain was very similar to the response following lobotomy—an indifference to pain. The patient admitted to pain only on direct questioning.

The topectomy performed is essentially the same as that used for psychiatric disorders. The portion of the cortex resected approximates areas 9 and 10 bilaterally. It may be said that the cortical area related to the effective response to painful stimuli is being narrowed down. The results would indicate that topectomy for the relief of pain is superior to lobotomy; there is little apathy or shock and little or no mental deterioration.

DISCUSSION

DR. ROY R. GRINKER: Dr. Tinsley has asked me to discuss this paper, not so much with reference to relief of pain as from the point of view of the psychoses that have been treated by topectomy. Areas 9 and 10 are not easily located, since they are not stimulable. Dr. Bailey has clearly shown that they are not even to be differentiated microscopically from other prefrontal areas. The surgeon is therefore unaware of which gyri he is removing or undercutting and to what degree. The psychiatrist is even more helpless, for he does not know the type of patient he should recommend for topectomy. Actually, a wide variety of psychotic patients have been subjected to this operation, usually on the basis of their intractability to other forms of treatment, such as psychotherapy of all kinds, electric shock and insulin shock. The conditions have ranged from the impulsive neurosis with psychopathic acting-out behavior to the severe chronic depression or schizophrenia with varying syndromes. The strange thing about the results of the operation is that no matter whether the patient has been impulsive, aggressive or deeply depressed, he tends to become, with relief, emotionally the opposite of what he was in his original psychosis. A depressed patient who all her life had conceded compliantly to her husband's tyranny became sufficiently overt in her hostility toward him

that she broke her toe in kicking him one day. She was able to release a great deal of aggressiveness that had formerly been inhibited. A patient with much anxiety, often increasing to panic, which caused wild, impulsive behavior, and at one time a leap out of the window because she feared an imaginary person was after her, became a placid person, unconcerned about her delusions.

In conjecturing about the effective mechanism of this operation, I should like to propose a hypothesis based on the known fact of relief of suffering associated with the preservation of pain. Pain is still experienced after the operation, but the aspect of suffering is no longer as intense. The patient, although reacting to all the neurological tests indicating adequate perception of pain, does not respond with the affective reactions that were so severely complained of before. We believe that the prefrontal areas as a whole have to do with some of the highest functions of the human being, actually with the most complicated sensitivity of that psychological function called the ego. The ego, which has control or command of psychomotor action, is also concerned with psychological perception. It is perceptive to internal tensions; it is perceptive to external significant cues. It could be stated that after topectomy the ego is less sensitive to pain from its superego's pressures, as in the depressions. The superego tension is there, but it is not perceived as painful and depression is reduced. The ego is less sensitive to the strength of the impulsive drives that seem to come from disturbances within the deeper level of the personality. I say less sensitive, because these impulses are still there. The person who impulsively acted out her psychosis still talked about what she would do but never went into action, being seemingly more apathetic and less concerned with the pressure. There seemed to be less of an awareness of the necessity of going into action. One can hypothesize that whether the pain is physiological pain or psychological, from stimuli which impinge on the organism from within or on its surfaces, the perception of this pain is still present after the operation, but the suffering and intense reactivity to these pains are no longer present.

DR. PERCIVAL BAILEY: It is quite clear to me that patients whose frontal lobes have been mutilated complain less of pain than do patients with normal frontal lobes. That one is closing in on the area responsible is not so clear to me. It is known that in psychotic patients removal of a certain amount of tissue from the anteromedial portion of the hemispheres gives approximately the same result. Penfield has demonstrated that removal of the same amount from the lateral portion of the frontal lobe and others have shown that removal of the same amount of tissue from the orbital tissue give a similar relief from pain. To my knowledge, no one has removed this amount of tissue from the orbital region in cases of pain, but I suspect that the result would be the same. It does not follow, therefore, that because one gets these results one is closing in on the area responsible. I suspect it is simply a matter of the amount of tissue which is removed from that area of the cortex which is connected with the dorsomedial nucleus of the thalamus—that is, the entire frontal lobe anterior to the agranular cortex.

DR. JULES MASSERMAN: Suppose we grant, for the moment, that the results of topectomy are favorable; even then, might they not be obtained by somewhat less heroic methods? Is it not possible to dispense with the primitive devices of trephine, bone saw and scalpel and use more modern gadgets? I understand they have such a gadget, called a betatron, at the University of Illinois which is capable of developing some 20,000,000 volts and destroying tissue 3 cm. below the surface, with relatively little damage to the skin. Would it not be possible, then, to have a "bloodless topectomy," as a physical form of what psychoanalysts like to call depth therapy? Would it be possible to experiment with animal brains first, then human brains? If direct exposure causes too much diffraction and tissue damage, tangential exposure of the cortex alone—perhaps areas 9 and 10—might be the solution. I understand Dr. Bailey is investigating that problem. Would he care to comment?

DR. PERCIVAL BAILEY: We have already started work with our betatron on rabbits, and we expect ultimately to go on to cats and monkeys and finally to man. However, it is not easy to control the depth of the penetration and the scattering. There is also the possibility of producing the same effect by destruction of the dorsomedial nucleus with an electrolytic needle; various stereotaxic instruments are being devised for this purpose.

DR. MILTON TINSLEY: Dr. Wycis, in Philadelphia, has been inserting a needle with the stereotaxic machine and coagulating the thalamic area of the brain. From what I read in *Time*, the results are very favorable in treatment of the painful states and of psychoses.

An excellent review of the literature on the effect of lobotomy in the psychotic patient appeared in the last issue of *Newsweek* (**34**:51 [Dec. 12] 1949).

The Struggle for Equilibrium. Dr. Meyer Solomon.

The living human machine is in a state of moving, dynamic, unstable equilibrium. Forces and processes arising within the individual human machine are frequently in conflict with other and/or external forces and processes. There result states of relative disequilibrium, tension, stress, strain and friction. States of equilibrium are accompanied with feelings of what are variously called satisfaction, equilibrium, stability, ease, poise, comfort, relaxation, equanimity, calmness, serenity, harmony and pleasure. States of disequilibrium are accompanied with feelings of what are variously called annoyance, disequilibrium, imbalance, unrest, uneasiness, restlessness, tension, strain, discomfort, dissatisfaction, disharmony, insecurity and unpleasure.

Human beings are thus subject to states and feelings of excessive strain and tension, of varying intensity and duration, arising from several types of causes. In the struggle to gain release from excessive tension and to maintain or regain equilibrium, they resort to various types of activity, normal and abnormal. The need for gaining release from excessive tension presents a situation comparable to that of a caged or trapped animal, as in the maze experiment, in the war neuroses and in prison psychoses.

Some common ways and means of gaining equilibrium were mentioned. The relation to other views was pointed out. The author emphasized the importance of the principle of equilibrium in the interpretation of human behavior and its possible application to the study and management of personality and behavior disorders. The views are in harmony with current scientific thinking in physics, chemistry, biology, physiology and psychology.

DISCUSSION

Dr. Jules Masserman: Dr. Solomon, in his own calmly profound way, attempts to quiet some of our current sounding of trash and tinkling of symbols (if I may paraphrase Corinthians XI: 15) by reminding us that all activity is but an attempt to regain physiological equilibrium, whether this be formulated in terms of the neurological hierarchy of Sherrington or the somatic homeostasis of Claude Bernard and Walter Cannon. Dr. Solomon might have gone on to point out that thus also the philosopher advises us to strive for a platonic balance among the vegetative, animal and rational aspects of the "psyche" ("id," "ego" and "superego," in more modern freudian mythology), that the Hegelian dialectician seeks a mode between logical opposites and that the theologian's greatest promise seems to be a Nirvana of restful surcease from all want and yearning. In any case, Dr. Solomon, despite a side trip into the paradoxical thesis that man "may come to seek states of tension in order . . . to seek release therefrom," returns to the clinical proposition that it is essential to resolve disturbing stresses and tensions in the therapy of various "neurotic" aberrations, ranging from abasia to zoophobia.

With this proposition I believe we can all, up to a point, register theoretical accord; indeed, stated somewhat differently, I have in my own writings equated biodynamic disequilibrium with all conation, whether called instinct, drive, desire, need, wish or other forms of covert motivation. Certainly, in the practice of medicine—and psychiatry will always, I hope, be a branch of medicine—we as physicians seek to relieve pathogenic stress in order to restore the harmonious function of the whole person and thus effect what we call a cure. Yet I would welcome Dr. Solomon's comment on certain heuristic, theoretical and operational difficulties with the concept of equilibrium as a transcendent principle of behavior. My own time permits me little more than a verbal gesture toward three of these difficulties as they arise in the laboratory, the library and life in general.

First, in clinical, and even in experimental, reasoning there is danger of a form of cyclic error which first presumes the "existence" of a "need" because certain behavior patterns "denote" it, then secondarily "explains" the behavior itself by the putative need. This error is inherent in the so-called hormic psychologies: McDougall, for instance, postulates an "instinct of gregariousness" from various social phenomena, then states that this instinct "causes" people to be gregarious. An even more subversive presumption may creep into experimental interpretations and be combined with unconscious wishfulness to produce highly significant

errors of observation and judgment. Thus, about a decade ago an experimental psychologist reported that depancreatized rats, actuated by their supposed hypoinsulinism, spontaneously selected a diet exactly suited to compensate for their diabetic disequilibrium. Strangely, however, the diet they selected, though considered perfect in 1935, would now be regarded as quite inappropriate to the disease. It would be of interest to have this work repeated today, presumably on rats abreast of the current literature.

Second, the concept that all action results from disequilibrium has even broader conceptual difficulties, which cannot be logically dissipated by the semantic device of reciprocal definition. Actually, modern chemistry (Urey) has undermined the concept of a static molecule; modern physics (Fermi) has abandoned the idea of a stable atom, and modern astronomy (Eddington) has surrendered even the semblance of a definable universe. Thinkers from Heracleitos to Bergson have turned instead to concepts of change, of evolution, of an eternal becoming, which is an expression, not of a transient disequilibrium, but of the fundamental essence of dynamic being.

In the last analysis, nevertheless, we all prefer to be physicians rather than metaphysicians, and the test of the thesis is in the therapy. But by this criterion, also, the equilibration theory creates more difficulty than it solves, since it confronts one with the startling proposition that all action is, etiologically, the result of literal dis-ease and is thereby in a sense, pathological. But is it not a highly commendable type of "dis-eased" action that, for instance, led to the fertilization of the ova from which we all sprang? And if, as Dr. Solomon implies, the embryo is really closest to balanced contentment, why does it, too, change and grow? Is is not also a praiseworthy type of discomfort which led Dr. Solomon to publish his paper on equilibrium in the *Journal of Abnormal and Social Psychology* (**19**:334, 1934), some fifteen years ago, and to revise it for our consideration tonight. In short, must we not distinguish between potentially constructive and destructive forms of disequilibrium? If we do not, may not our therapy, while possibly relieving our patient's inner anxieties and outer aberrations, leave him an inert, unproductive citizen—an apathetic, rather than a happy and creative person?

I am sure that Dr. Solomon has had all of these considerations in mind, so that perhaps the main purpose of my remarks has been to present him with an opportunity to comment further on his interesting thesis.

DR. MEYER SOLOMON: I think Dr. Masserman and I agree basically. I did not say that all activity is but an attempt to regain physiological equilibrium. It is, rather, an attempt to maintain or regain such equilibrium. I did not use the term "need" as applying to the levels of activity of the lower animals. That would be an anthropomorphic approach, attributing to such low level activities conscious purposes—truly a conception of the world as will and idea. I would speak, rather, of the "tendency" toward equilibrium. I may say that originally, in his conception of dreams, Freud talked of "wish fulfilment," but in one of his later writings he admitted that it would be more correct to describe dreams as "attempts at wish fulfilment." He would have been nearer the truth had he spoken of "attempts at" or "tendencies toward" equilibrium or balance. However, limiting the discussion to neuropsychiatric patients, I may say that they do feel the need or craving for equilibrium or balance. That is why they come to the physician. If the physician asks the usual patient what it is he wishes for most, what he is really coming for, he will say: "Doctor, I want peace, calmness, poise. I am struggling for peace of mind and body. I want to be relaxed, at ease."

As to Dr. Masserman's second point: Ceaseless activity seems to be at the basis of all seemingly passive phenomena. Bergson, in his "Creative Evolution," stressed this philosophy of change. Spenser spoke of the instability of the homogeneous. There is a flux between disequilibrium and equilibrium, activity and passivity. The human organism is in a state of dynamic unstable equilibrium.

As to Dr. Masserman's third point: I did not mean to imply that the goal is to gain and maintain equilibrium at all costs, since that would mean that one should always fit into conditions as they are and accept and submit to them. A period of profound upheaval or disequilibrium is often most essential and beneficial in order to bring about reorganization and integration at a new level. Such periods have been necessary and are, I presume, responsible for mutations, changes in evolution and development; progress in life in its individual and social aspects has been in large measure dependent on changes of that nature.

From a practical point of view, aside from the pros and cons of the all-embracing inclusiveness of the disequilibrium-equilibrium conception, the problem of psychiatry is fundamentally and essentially to help the patient get into a better state of psychophysiological balance or equilibrium, by various methods.

Much of the misunderstanding and confusion in the field of psychiatry has been due to the use by various writers, especially Freud and his followers, of terms with vague, multiple meanings, such as wish, pleasure and the unconscious. If Freud had been more cautious in his use of terms and had employed those with a wider and more inclusive meaning, such as balance and equilibrium, there would not have been and would not now be, all this confusion, chaos and conflict in the field of psychiatry. This is not to deny the many valuable contributions, direct and indirect, of the Freudian school and its offshoots. This criticism applies also to many of the other writers who endeavored to fit all activity into concepts that were not in accord with scientific principles. The theory of equilibrium is, in my opinion, in harmony with current trends in other scientific disciplines, especially the basic sciences of physics, chemistry, biology and physiology.

Fourth International Neurological Congress, Paris—Sept. 5-10, 1949. DR. GEORGE B. HASSIN.

The Fourth International Neurological Congress, which was held in Paris, France, had an enrolled membership of 1,059 active members and 300 associate members. There were no delegates from Russia, China, Japan, Germany, Yugoslavia or Bulgaria, and only a few scattered delegates represented Czechoslovakia, Poland and Rumania. In short, about a billion people have not been represented, and for this reason the Congress cannot tbe considered international. The largest number of delegates came from the United States (104) followed by England (157) and the Netherlands (75). The official languages were English, French, Spanish and Russian. Though the Congress was only partly international, an abundance of papers (about 350) were listed for presentation; but many of them were presented by title, as the scheduled authors did not appear. The leading topics pertained to electroencephalography, the optic thalamus, viral diseases, surgical treatment of pain, and epilepsy, while the special topics covered almost every phase of organic neurology. Some were of unusual interest; but, unfortunately, it was possible to attend only a small portion of meetings, as from 8 to ten sessions were taking place simultaneously. The sessions were very informal. The names of the discussants were not announced; no time limit was set for presentation; closing comments were for the most part not obligatory, and no stenographic or other recording was done. One was impressed with the magnitude of the amount and variety of contributions, "orations" and special discussions of certain topics; and one wondered what would have been the situation if delegates from the other half-world had not absented themselves.

Especially well managed were the several social phases of the Congress, in which not only the delegates but also their relatives and friends, participated. In addition, there were the city of Paris and its environments, with their rich historical background and intellectual and cultural associations and the opportunity of coming into personal contact with a number of highly interesting personalities.

Alex J. Arieff, M.D., *President in the Chair*

Regular Meeting, Jan. 10, 1950

Ipsilateral Sensory Loss Following Chordotomy: Report of a Case. DR. HAROLD C. VORIS.

A white woman aged 46 with intractable pain of the right lower extremity was subjected to left unilateral anterolateral chordotomy at the level of the sixth thoracic vertebra. During the course of the operation it was discovered that, while there was no sensory loss on the right side, there was analgesia to pinprick below the umbilicus (tenth thoracic segment) on the left.

A month later right unilateral anterolateral chordotomy was carried out and extended to a complete section of the right anterior quadrant of the cord. This produced analgesia to pinprick

on the right between the umbilicus and the anterior aspect of the knee, with preservation of sensation in the lower lumbar and sacral dermatomes. This analgesia on the right later became hypesthesia to pinprick, but the analgesia on the left remained permanent.

The author stated that he knew of no similar case in the literature except the one reported by French and Peyton (*J. Neurosurg.* **5**:403, 1948). They felt that a congenital anomaly, a modified diplegia of the cord, was the most probable explanation of the anatomic variation but did not ascertain the presence of such an anomaly.

No evidence of lamellation of the uncrossed pathway for pain sensation on the left was noted. On the right the fibers carrying pain sensation from the sacral and lower lumbar dermatomes were located more mesially or superiorly than those representing the trunk. This is the opposite of the lamellation in the normal lateral spinothalamic tract. It is suggested that uncrossed ascending sensory neurons, whether primary or secondary, might be expected to group themselves, with the fibers representing caudal dermatomes, superficial to the fibers representing higher levels.

Nerve Regeneration in Grafts. Dr. Frederick Hiller.

The demonstration of 25 original Kodachrome® photomicrographs shows that the neurotization of grafts follows the same principle as that found in cases of nerve injury. In both conditions nerve fibers may regenerate within the original endoneurial tubes, the continuity of which has withstood trauma or transplantation in the form of a graft. This occurs in mild contusions which damage or destroy the nerve fibers, as well as in certain autogenous grafts whenever the mesodermal endoneurium survives. The outcome is an isomorphous neurotization which resembles the neurotization of a distal nerve segment after secondary degeneration, but which differs by an endoneurial fibrosis, a characteristic disfiguration of the myelinated axons and hyperplasia of unmyelinated nerve fibrils. In severe nerve trauma or in certain grafts, mostly homogenous ones, tissue destruction or autolysis disrupts the continuity of the endoneurial tubes. Here the regenerating nerve fibers with their Schwann cells follow the proliferating mesodermal cells and fibers, forming a neuromatous tissue. The neurotization is, and remains, heteromorphous. In homogenous grafts the additional perineurial and epineurial neurotization leads to complete obliteration of the primary structure of the graft.

The neurotization of grafts in man follows the same principles. The greatest obstacle is the tendency to formation of dense collagenous scar tissue. This may be obviated by using grafts not longer than 5 cm. and, if necessary, by successive grafting. Autogenous cable grafts should be superior to homogenous grafts, but homogenous grafts obtained from the newborn infant ought to be tried.

DISCUSSION

Dr. George B. Hassin: The beautiful slides shown by Dr. Hiller well demonstrate regenerated nerve fibers streaming among numerous structures of the graft from the central stump to the periphery. The question arises as to what pathways the young nerve fibers follow in the graft to reach the peripheral stump. In a peripheral section of a divided nerve fiber, the axons and myelin are destroyed, leaving, as is generally assumed, an empty tube through which the regenerating nerve fiber travels. This is nonsense, as no empty spaces are created or exist in tissues. Boeke assumed that the regenerating nerve fibers extend along or within the cytoplasm of Büngner's bands. However, this could not be satisfactorily demonstrated. Another question is what becomes of the graft. The graft remained in the nerve for from a few days to about two years or longer. There was thus an excellent chance to follow the morphological changes that had been taken in the graft in both early and late stages. What has autolysis to do with the fate of the graft?

Dr. Victor Gonda: Dr. Hiller stated that after three years the functions returned. Will he tell us which functions returned and describe the means he used to ascertain the return of function?

Dr. Frederick Hiller: Let me clarify a point on which I possibly did not make myself clear. I did not mean to say that there was restitution of function after three years in the specimen presented. What I did was to show a specimen in which grafting had resulted in full restitution of function and which was removed for study about three years after implantation. As to testing for restitution of function, I am happy to say that we have as our guest my

co-worker in this experiment, Dr. George Perret. Dr. Perret has done the clinical testing in these cats, and I am sure he will be happy to answer the question.

DR. GEORGE PERRET: Our method of examination of these animals, including testing of function, was published fully in *Surgery, Gynecology & Obstetrics* (**80**:35-59, 1945). We tested function by evaluating the spontaneous motor responses of the involved extremity on painful stimulation of the animal. We studied the animal's stance and gait. We examined return of sensation to pinprick in the areas of distribution of the repaired sciatic nerve and the return of reflexes in the involved extremity, and we found in the animals who had recovered completely normal fanning reflex of the toes, step reflex of the foot and ankle reflex. Finally, we tested the responses of the extremity on direct electrical stimulation of the nerve above the site of the graft, on the graft and below the graft.

DR. FREDERICK HILLER: As to Dr. Hassin's question about regeneration of grafts and the kind of pathways which the regenerating nerve fibers take, let me repeat that I fully realize that it is ever so much more difficult for you to see the details than for some one who has examined these, and sounder, pictures for years. Wherever the endoneurial tubular structures survive, as in "isomorphous neurotization," the nerve fibers regenerate within these preformed pathways. Where they have perished, nerve fibers must have a scaffolding on which they grow, and this scaffolding is furnished by proliferating mesodermal cells and fibers. Nerve fibers do not necessarily grow toward the distant segment. I have shown in several photographs that nerve fibers sometimes lose their way completely, particularly in homogenous grafts; they turn around the graft and enter the epineurium of a nerve. One frequently sees nerve fibers growing wildly in adhesions around the graft, from whence they may penetrate between muscle fibers. It is a fact that the perineurium behaves similarly to the immature endoneurium of a regenerating nerve, seeming to indicate that all kinds of immature cells of the stroma may participate in leading regenerating axons. I have said that it is very difficult to distinguish immature mesodermal cells from Schwann cells, and I think every one, including men like Doinikov, who is an experienced neurohistologist, has made this observation. All immature cells look very much alike, and a cell can be identified as a Schwann cell only when it has acquired the typical shape and the relation to the axon which is characteristic of Schwann cells. One case in particular, that of a homogenous graft, one hundred and five days after implantation, shows convincingly what becomes of a graft and how neurotization proceeds. In this case there was a large necrotic area in the graft, as happens so often in human grafts, especially in the central portion. There one saw how macrophages clear up the debris; they prepare the way for the mesodermal organization. In their wake follow fibrocytes, and as soon as the scaffolding mesodermal stroma is established, nerve fibers with Schwann cells appear and follow the lead of the collagenous fibers. Nerve fibers seem to follow surfaces, which, as one sees ever so often, may be simple strands of fibrin or, as I have described it in nerve injuries, as well as in grafts, mesodermal fibers. This is the way in which I assume, and I think I have shown, that grafts become organized. The difference between an autogenous graft and a homogenous graft is simply that in the former—at least in favorable circumstances—the endoneurial tubes survive, the old endoneurium proliferates and it is within the syncytial bands of their leukoblasts that the regenerating nerve fibers arrange themselves in a parallel course. Where the original endoneurial structure does not survive, as in places where, as in most homogenous grafts, at least partial tissue necrosis occurs, proliferating fibrocytes with their fibers determine the course of outgrowing axons, which in the syncytial medium of Schwann cells fill the interstices of the mesodermal stroma. These two aspects of regeneration in grafts I call isomorphous and heteromorphous neurotization.

Clinical Use of Radioactive Diiodofluorescein in Diagnosis and Localization of Tumors of the Central Nervous System in One Hundred and Five Consecutive Patients. DRS. LOYAL DAVIS, JOHN MARTIN and MOSES ASHKENAZY.

On a series of 105 consecutive patients suspected of having tumors of the central nervous system, studies by means of radioactive diiodofluorescein revealed 95 per cent accuracy in diagnosis of lesions verified surgically or by pneumography. On this basis, it would seem that the radioactive diiodofluorescein tracer test is a simple, safe, painless and reliable method for the localization and diagnosis of cerebral tumors.

The technic was simple, and instrumentation consisted of a Geiger-Mueller tube, a counting rate meter and a mechanical graphic recorder.

There was 93 per cent accuracy in localization and diagnosis of the 60 histologically verified tumors of the central nervous system, which included 26 gliomas, 8 meningiomas, 10 metastatic carcinomas and sarcomas, 3 tumors of the pituitary gland, 6 tumors of the spinal cord, 2 cerebellar hemangioblastomas, 1 acoustic neurinoma, 2 subdural hematomas, 1 cerebellar cyst and 1 metastatic cerebral abscess. A positive result in the radioactive dye test was recorded in 5 of 6 verified tumors of the spinal cord.

The affinity of radioactive dye for tumor tissue was related not only to the degree of malignancy or cellularity but also to the vascular pattern of the tumor. The more malignant the neoplasm, the greater was the concentration of radioactive fluorescein. There was relatively little, or no, concentration of dye over the sites of large cysts or chronic subdural hematomas.

The "negative" findings also proved to be 95 per cent accurate and were of equal importance in the differential diagnosis of cerebral neoplasms, especially from such lesions as idiopathic or post-traumatic epilepsy, hypertensive cerebrovascular accidents, multiple sclerosis, perichiasmal arachnoiditis, meningovascular syphilis, ruptured intracranial aneurysm and psychosis or anxiety states. It proved of greatest value in the differential diagnosis of papilledema and of jacksonian epilepsy.

Localization proved to be much more precise than with electroencephalography or pneumography whenever verification was obtained at operation or at autopsy. Pneumography revealed an 80 per cent accuracy, and electroencephalography revealed only a 60 per cent accuracy.

Tumor recurrence could be demonstrated readily with this technic. Postoperative high voltage radiation therapy caused an increased concentration of radioactive diiodofluorescein in the more malignant intracerebral neoplasms.

Special technics of counting have been evolved, so that the accuracy in localization of midline tumors, such as those of the pituitary, brain stem or posterior fossa, is as good as that of localization of the more superficially situated cerebral neoplasms.

DISCUSSION

DR. ROLAND P. MACKAY: What is the fate of the diiodofluorescein, and is there any danger in its use?

DR. PERCIVAL BAILEY: It is impossible to judge a paper like this without having gone through the records oneself. I can believe, and it seems logical to me, that one can localize a neoplasm by this method, but that one can make a pathological diagnosis I would have to be convinced. That one could make a differentiation of meningioma from astrocytoma does not seem to be logical. I remain a little skeptical about that possibility.

DR. GEORGE PERRET: Angiography has hardly been mentioned in this paper. I should like to know whether or not studies have been made comparing carotid arteriography with this new diagnostic method, so convincingly presented by Dr. Ashkenazy, and what relation exists between these two diagnostic procedures. How can one differentiate between a malignant tumor and a cortical or subcortical arteriovenous angioma, for instance?

DR. GERHARDT VON BONIN: I should like to know how much a millicurie is in cubic centimeters. Is it 10 or 1 cc.? What is the half-life value of diiodofluorescein? Does the test have to be done rapidly?

DR. IRVING SHERMAN: Is this radioactive substance taken up by the tumor cells themselves, or is it simply concentrated in the radioactive substance in the blood of the tumor?

DR. MOSES ASHKENAZY: In answer to Dr. Mackay's question about the fate of the dye: Diiodofluorescein is rapidly excreted through the kidneys, through the liver and through the salivary and sweat glands. As a matter of fact, several recent investigators, particularly Drs. Parker and Menaker, gave a recent paper at the meeting of the American College of Surgeons in 1949 in which they utilized the excretory functions of the fluorescein as a test of hepatic function and bile excretion during the operation.

We believe that there is no significant hazard to the patient through the use of radioactive fluorescein in amounts of 1 to 2 millicuries, for studies of the distribution and excretion of this dye have been made in human subjects, dogs and rats and the biologic half-life in man

was found to be only two to three days. The amount of radiation to the skull is roughly no more than that received in a series of roentgenograms or encephalograms. The dose of radiation to the thyroid is substantially less than that received by patients tested with the smallest amount of radioiodine in studies of thyroid function.

In answer to Dr. Bailey's question, I wish to state that we have made notes of the definite relation which exists between the vascularity and cellularity of the tumor and its radioactive dye concentration. We mentioned only the possibility of determining in a general fashion the relative degree of malignancy of the tumors involved and stated that this might be feasible in the future with instruments of higher detection value than the present ones, and perhaps with more sensitive, yet to be discovered radioactive dyes. That the relation exists is a fact which we discovered when we correlated the microscopic characteristics of the tumors with the number of counts per minute obtained by external counting with the Geiger tube. We have not attempted to make a pathological diagnosis; we have only made note of this very pertinent relation between the vascularity and cellularity of the tumors and their radioactive dye concentrations. We have noticed in every instance that the more malignant the neoplasm, the greater was the concentration of radioactive fluorescein.

In answer to Dr. Perret's question about angiography, several such studies have been made and the results correlated with those of studies with radioactive dyes. In three cases of subarachnoid hemorrhage secondary to a ruptured intracranial aneurysm, as verified later by angiography, the radioactive dye test gave normal readings. Because of the presence of papilledema, a tumor was suspected. One of the patients even had a craniotomy, since not only angiography, but pneumography and electroencephalography, pointed to a space-occupying lesion of the right frontal lobe. However, at operation no tumor was revealed, but an aneurysm of the anterior cerebral artery was visualized on the floor of the anterior cranial fossa, as well as multiple areas of old intracerebral hemorrhagic softening. In answer to Dr. Perret's second question, it is easy to differentiate a malignant tumor and an arteriovenous angioma. As I stated earlier, the radioactive dye concentrations are intense in the case of malignant tumors, mainly as a result of the increased vascularity of the peripheral capillaries and the disturbed permeability of their endothelial walls. Since an arteriovenous angioma involves vessels of larger caliber with muscular walls, radioactive dye cannot permeate, and hence the concentration over such a lesion is very slight as compared with that of a malignant neoplasm, with its striking proliferation of capillaries and the obvious disturbed permeability of their endothelial cells. This, of course, accounts for the pronounced cerebral edema so frequently seen surrounding glioblastomas and metastatic carcinomas and sarcomas and, hence, for the very high differential counts of the radioactive dye in such instances.

In answer to Dr. von Bonin's question, the number of millicuries injected remains the same and is approximately 1 to 1.2 millicuries. The volume varies, since the half-life of I^{131} is eight days. A simple table has been prepared by the Atomic Energy Commission which makes it easy to figure out the exact number of cubic centimeters necessary to contain 1 millicurie of radioactive dye. The most significant counts occur within one-half to two hours after the intravenous injection of the radioactive diiodofluorescein. At the end of three to four hours, the readings are only confirmatory, for the differential concentrations are no longer striking.

In answer to Dr. Sherman, there is no definite evidence that the radioactive dye is taken up by the tumor cells themselves. However, studies with acid-diffusible dyes other than fluorescein on neoplastic growths in lower animals, by such men as Ludford and Duran-Reynals, indicate that the foreign dyes localize selectively in cancer tissue—not in the cancer cell itself, but in the internal cellular stroma, probably as a result of the altered permeability of the stromal blood vessels. Duran-Reynals even believes that this abnormally high permeability of endothelial cells, leading to the escape of dye, may be increased by the so-called spreading factor of cancerous tissues. The dye does not remain in the blood, since studies on dogs revealed that within 30 minutes only 1 per cent of the injected dye remains in the blood stream itself. It is usually taken up quickly by the liver and kidneys and excreted through the bile and the bowel and also through the urine. Our studies seem to bear out this hypothesis; namely, that the radioactive dye concentrations are dependent on the vascularity of the lesion, and particularly on the state of their capillary endothelium.

Alex J. Arieff, M.D., *President in the Chair*

Regular Meeting, Feb. 14, 1950

Recent Contributions to Knowledge of the Cerebellum. DR. RAY S. SNIDER.

Tactile, auditory and visual areas are known to exist within the cerebellum. Motor, tactile, auditory and visual areas in the cerebral cortex project to these same cerebellar areas, which, in turn, project back on the cerebral areas. Certain areas of the cerebellum when properly stimulated produce localized movements, suppression or facilitation of cortically or reflexly induced movements. Cerebellar stimulation may modify cerebral activity.

A new concept of function is developed which includes cerebellar action in dampening and potentiating associated sensory and motor centers alike.

DISCUSSION

DR. PERCIVAL BAILEY: I have watched the work of Dr. Snider with great interest. It has been done with meticulous accuracy and considerable imagination. If I make bold to discuss his work, it is only because the subject has interested me for many years, although I have never attempted to solve any problems connected with the cerebellum by experimentation.

I first became interested in trying to explain why medulloblastomas often did not produce nystagmus and very little asynergy of the upper extremities. The results of that attempt can be found in the chapter on medulloblastoma "Intracranial Tumors" (Springfield, Ill., Charles C Thomas, Publisher, 1933). In most modern treatises on neurophysiology present day ideas are traced back to Larsell. But the conception of the fundamental subdivision of the cerebellum into archicerebellum, paleocerebellum and neocerebellum was clearly formulated by Sven Ingvar in his Herter Lecture (*Bull. Johns Hopkins Hosp.* **43**:315-337, 1938). For many years physiologists tried to use for the cerebellum the methods of extirpation and stimulation which had been so fruitful in the study of the cerebrum, but it was not until Ingvar, a comparative anatomist, showed the way that their efforts began to bear fruit. Histological study of the cerebellar cortex gave no clue, as had that of the cerebral cortex, since the intrinsic structure of the cerebellar cortex is uniform throughout. There is nothing comparable to the striate area or the giant cells in the cerebellum; so the cerebellum boasts no Gennari and no Betz cells. The differentiation of function in the cerebellum depends on its external connections and not on differentiation of internal structure of the cortex.

In line with the dictum of Hughlings Jackson that differentiation of structure means differentiation in function and that difference in function implies difference in structure (if one thinks only in terms of the intrinsic structure), one might expect that the cortex of the cerebellum would have a uniform general function. The first to attempt to formulate this general function was Babinski, who (Transactions XVIIth International Congress of Medicine, London, Section XI, 1913, pp. 1-59) conceived its action to be that of a brake. Today the same ideas expressed in terms of a negative feedback of servomechanisms (Bailey, P., in Bucy, P.: Precentral Motor Cortex, Urbana, Ill., University of Illinois Press, 1949, chap. 10).

The most obvious action of the cerebellum is on the skeletal musculature, and for this reason Sherrington spoke of the cerebellum as the head ganglion of the proprioceptive system. The first to extend knowledge of the regulating action of the cerebellum was Moruzzi, who showed that it regulates also autonomic functions. Now Dr. Snider demonstrates clearly that it enters also into tactile, visual and auditory reactions. To return to comparative anatomy, it is interesting that the portion of the vermis concerned with visual and auditory connections is that portion which develops last, simultaneously with the cerebellar hemispheres.

So one finds the cerebellum modulating all sorts of nervous mechanisms, acting in the manner of a feedback, or servomechanism, the locus of its action depending not on its intrinsic structure but on its connections. Just how its peculiar internal structure lends itself to its general function is unknown, but Dr. Snider is attacking this problem also; and, if past performance is any guarantee, we may anticipate further insight into this problem in the near future.

DR. RICHARD B. RICHTER: Dr. Snider has indicated that he believes the relay pathway from the retina is via the superior colliculus. Does he believe that the auditory impulses are relayed via the inferior colliculus, and what is his idea as to the pathway taken by tactile impulses to the cerebellar cortex?

DR. WARD C. HALSTEAD: I wonder whether Dr. Snider has attempted to map a projection for the nonacoustic labyrinth on the cortex of the cerebellum.

DR. R. P. MACKAY: Although not a physiologist, I am impelled to comment on this stimulating paper. I am sure that Dr. Snider would not imply that the cerebellum is primarily involved in sensory phenomena and that he would not have us believe that one uses the cerebellum to see with. However, it appears to me that every afferent impulse which enters the nervous system has a proprioceptive implication. For example, if I see something to my left, that fact immediately implies a pattern of muscular tone appropriate to the stimulus. Similarly, a sound heard might be expected to induce an appropriate tonic pattern. Therefore, the cerebellum must in some way be involved as a whole or in part whenever any afferent impulse leads to a response. One wonders whether the activity recorded by Dr. Snider is only a reflection of the proprioceptive activity induced by such tonic changes. May I ask, therefore, whether the electrical changes observed were seen after interruption of afferent impulse from the muscles in which tonic changes might result from a stimulus? For example, would sensory impulses from the leg lead to electrical changes in the cerebellum if the dorsal columns were previously severed?

DR. GERHARDT VON BONIN: Years ago (I think about 70) Bubnoff and Heidenhain investigated the function of the cortex. They wondered how cortical excitation could ever die down again once it was stirred up. It occurred to me some time ago that for the motor area it would be possible to assume that the cerebellum (via cerebellocerebral pathways) could provide just that sort of soothing mechanism, or brake, in order to wipe the cortical slate clean again. I wonder if Dr. Snider agrees with me. As an anatomist, I see very clearly how the tactile area could come under the influence of the cerebellum. Has he any idea about the pathways from his cerebellar visuoacoustic area to the visual and acoustic areas of the cortex?

DR. RAY S. SNIDER: First of all, I want to thank Dr. Bailey for his pleasant remarks. As a matter of fact, Dr. Bailey has brought out older work on my pet subject that I was not aware of. I agree wholeheartedly with him that there is some basic mechanism which is being distributed to widespread centers.

Concerning the question of the auditory pathways, here are the data which I have: First, if large lesions are placed in the inferior colliculus, responses within the auditory area of the cerebellum are blocked. Dr. Niemer has evidence from chromatolysis studies which shows that a portion of the dorsal cochlear nucleus passes to the cerebellum. As a matter of fact, Cajal, in the early 1900's, demonstrated a pathway from the cochlear nucleus to the cerebellum in the mouse. It appears that nothing is new in the field.

As to the question of the tactile pathway, and again I must be cautious because of some of my anatomical colleagues, it appears that this projection may pass through the spinocerebellar tracts. My reason for thinking so is the remarkable similarity which exists between cerebellar areas receiving dorsal and ventral spinocerebellar fibers and the tactile cerebellar areas. However, I must add a word of caution, for no one has thoroughly investigated the possible role played by the external cuneate and the lateral reticular nuclei. The splendid work of Brodal and Jansen certainly indicates the necessity of investigating the latter.

Dr. Haistead asked about the nonacoustic labyrinth. I should like very much to get into that. Dow has investigated it, as you know, but it has not been an easy thing to do; so far as I am concerned, Dr. Dow has done the authoritative work on it.

Concerning Dr. Mackay's question as to the role of the proprioceptors, the auditory responses occur in the cerebellum of a spinal animal in which the fifth and seventh cranial nerves have been cut. They also occur in a decerebrate animal in which the inferior colliculi have been spared. Therefore, the cerebellum cannot be a spinal or a cerebral relay. If one conceives of the cerebellum as a center for integration of the activity initiated by other centers, then it the organism is to function smoothly the integrating center must be ready to respond when "called on" by the "initiator." That would fit into Dr. Mackay's concept of a tonic pattern, especially if applied to an appropriate motor response. However, a broader concept

must be adopted to account for the widespread projections to higher centers, especially in the cerebrum. In the case of the latter it is conceivable that the cerebellum acts to maintain a certain threshold level, or "tone" if you like.

Thank you, Dr. von Bonin, for your comments, but I must confess I cannot answer the questions; to me, the cerebellum may not only "soothe" a hyperactive cerebrum but may also "step up" a hypoactive one.

Ventriculostomy in Treatment of Obstructive Hydrocephalus in Children. Dr. Harold C. Voris.

The use of ventriculostomy in the treatment of obstructive hydrocephalus in infants and young children was discussed. In these small subjects the temporal approach, with rupture of the lateral aspect of the floor of third ventricle, as originally described by Dandy, is technically superior to the anterior approach of Stookey. The procedure has been used oftenest in the treatment of obstructive hydrocephalus associated with spina bifida and due to the Arnold-Chiari malformation. In the author's experience with this condition, ventriculostomy has been much more satisfactory than suboccipital craniectomy.

DISCUSSION

Dr. Louis D. Boshes: I wonder whether Dr. Voris has made any attempt to measure the intelligence of these children, since the question of the end results will always be raised.

Dr. Harold C. Voris: No psychometric studies have been carried out. The patient whose case has been described has been under observation for nearly three years and seems to be developing normally so far as cerebral function is concerned. She has, of course, a serious neurological deficit in the lower extremities. I did not discuss the indications for operation in cases of spina bifida. I would not operate on a child with spina bifida with evidence of the complete loss of function in the lower extremities. This child had apparently normal function in one extremity, and she apparently still has one normal lower extremity. Most patients have not been under observation long enough to permit any statements about how justifiable their salvage has been from the standpoint of cerebral function.

A Study of One Hundred and Eighty-Two Cases of Verified Astrocytoma, Astroblastoma and Oligodendroglioma of the Brain. Dr. Loyal Davis, Dr. John Martin, Dr. Frank Padberg and Dr. Robert K. Anderson.

From July 1, 1924 until Jan. 1, 1949, 972 intracranial tumors were verified microscopically. Of this number, 523 (53.8 per cent) were classified as gliomas; of these, 160 (16.6 per cent) were astrocytomas, 24 (2.5 per cent) were oligodendrogliomas and 5 (0.51 per cent) were astroblastomas. In each case the diagnosis was verified and the classification made by microscopic sections according to established histopathological criteria.

Statistical studies on the type and preoperative duration of symptoms were reported; the gross and microscopic observations in specimens removed surgically were correlated, and the operative results and time of survival were evaluated. The effects of postoperative high voltage roentgen therapy were demonstrated histologically, and the survival time of patients so treated was compared with that of subjects who had not had roentgen therapy.

It was felt that tumors composed of cystic masses carry a longer survival time than grossly solid tumors and that the solid tumors have more actively proliferating cells. Survival studies indicated that roentgen irradiation has little clinical effect on this general group of tumors. Very little tendency to dedifferentiation was noted. It is believed that the cell type of the tumor is determined early. Evidence indicating that pregnancy stimulates the growth of intracranial gliomas was presented. In general, the results indicate the value of determined surgical treatment of the gliomas.

DISCUSSION

Dr. Percival Bailey: This discussion follows generally accepted lines. I might point out that there are persons who believe that the astrocytoma which occurs in the cerebellum and that which occurs in the cerebrum should have different names; some pathologists maintain that astrocytoma of the cerebellum is not a neoplasm at all. I might point out also that the

percentage of astroblastomas will vary with the observer and there has been some question as to validity of this type. There are all degrees of transition between astrocytoma and glioblastoma, for both tumors arise from the same basic cell. A dividing line can be fixed almost anywhere on either side of the astroblastoma. One can have 5 or 15 per cent of astroblastomas. If one adopts the criterion that the perdominating cell should have a large process extending down on the vessel wall, the percentage of astroblastomas will be small. I should accept the diagnosis of all those tumors of which lantern slides were projected tonight, but I might point out that hematoxylin and eosin is not a satisfactory stain with which to identify oligodendrogliomas. One can identify them only with silver impregnation, and that is rarely employed; the method is rather difficult and does not always succeed. In the literature there are many wild statements about oligodendrogliomas, and I should say that whatever is written about them had better be accepted with a grain of salt.

DR. ROBERT K. ANDERSON: I want to say that I appreciate Dr. Bailey's discussion.

NEW YORK NEUROLOGICAL SOCIETY AND THE NEW YORK ACADEMY OF MEDICINE, SECTION OF NEUROLOGY AND PSYCHIATRY

Lewis D. Stevenson, M.D., *President, New York Neurological Society, in the Chair*

Combined Meeting, Jan. 11, 1949

Regeneration of the Cauda Equina Through Nerve Grafts: An Experimental Study in Monkeys. DR. I. M. TARLOV, DR. D. BERMAN, DR. J. MOLDAVER and (by invitation) DR. E. KELLERMAN.

In a series of 12 monkeys, segments of the posterior roots, varying from 3 to 51 mm. in length, were used to repair defects in the anterior roots of the cauda equina. Plasma clot, either autologous or homologous, was used as the suture material. Paralysis of the foot, the leg and, partially, the thigh followed the operation, after which the animal was followed for periods up to 25 months. Very good graft takes were observed on both macroscopic examination. Axis-cylinders readily crossed both proximal and distal suture lines. They were present abundantly within the graft. Normal numbers of axons appeared in the distal segment of the root and peripherally to the termination of the sciatic nerve. The axis-cylinders acquired myelin sheaths, and motor end plates reformed. Chronaxia studies showed evidence of progressive functional improvement in the extremities supplied by the grafted roots. Moreover, electrical stimulation of the roots above the level of the grafts 12 to 17 months after operation resulted in forceful contraction of the reinnervated muscle groups.

In monkeys observed for periods up to 25 months after operation functional recovery of the paralyzed limb has not occurred. However, this seems to be due to the severe ulcerations, contractures and muscular atrophy that inevitably occurred. In man, whose muscles and joints can be cared for properly after injury, by massage, limb exercises, galvanic stimulation of the muscles and other forms of physical therapy, combined with adequate general nursing care, it is believed that conditions would be much more favorable for the recovery of function. The operation would not, of course, restore sensory function. To effect some return of sensation to the anesthetic parts, intercostal-lumbosacral nerve root anastomosis by means of posterior root grafts was carried out in monkeys. Excellent histological regeneration of nerves through grafts 9 cm. in length has been obtained. The experimental evidence shows that these nerve-grafting procedures are indicated in man in an attempt to effect return of sensory or motor function when severance of the cauda equina has occurred.

DISCUSSION

DR. BYRON STOOKEY: Dr. Tarlov and his associates have done a tremendous amount of work. I wonder, as I imagine he does, just how this can be applied to the human being. One sees few cases in which such a procedure would seem applicable.

I have several questions. Has Dr. Tarlov any cross sections of the sciatic nerve distal to the point of section to show that the whole of the peripheral nerve had degenerated as a result of dorsal root section, such as he has done? The number of roots which go into the formation of a plexus is variable; consequently, it is essential to establish the fact that

all the innervation has been destroyed by section of the roots he has chosen for his experiment. Since he has relied on the presence of nerve fibers in the peripheral nerve distal to the section to prove that regeneration through the transplant has taken place, it is imperative to demonstrate in several animals that as a result of section of the dorsal roots all the nerve fibers in the peripheral portion of the sciatic nerve have undergone degeneration. The presence of nerve fibers distal to the transplant within the nerve trunk would hardly be valid evidence of regeneration unless previously he had proved that no nerve fibers were present in the peripheral stump.

I should like also to ask what was done to determine the source of the smaller fibers seen in the sections of the distal segments. It should be proved that they were not postganglionic fibers, because the postganglionic fibers enter the peripheral nerve outside the dural sac and become a part of the peripheral nerve distal to the point of nerve graft, and the fibers seen distal to the nerve graft may therefore be nonmyelinated postganglionic fibers. Unless the sympathetic system contributing to the peripheral nerves was eliminated, these fibers would appear intact within the distal nerve segments. Therefore, on the basis of the presence of intact nerve fibers in the distal nerve stump, none of the experiments could be accepted as establishing that regeneration had taken place.

The problem as presented, showing that a nerve graft can be made to transmit nerve fibers, has already been amply demonstrated in the experimental work that was done in World War I, and I am glad to see that the experimental work of Dr. Carl Huber and his associates which demonstrated in experimental animals that nerve grafts can be made to transmit nerve fibers from the central to the distal stump has been confirmed. This work has been amply demonstrated and proved experimentally. In my own work, I have seen nerve grafts function after transplantation of a segment of the radial nerve into the posterior interosseous nerve in 2 cases. The graft must be not too large, so that central necrosis does not take place.

I shall look forward to Dr. Tarlov's further experimental work in this field.

DR. HENRY ALSOP RILEY: It seems to me that in any attempt to study nerve regeneration in the cauda equina by means of study of end plates one would run into the complication of the rearrangement of fibers in the lumbosacral plexus unless one cut all the roots entering into the formation of the plexus. The same thought also occurred to me that the finely myelinated fibers may represent the fibers derived from the sympathetic nervous system. I wonder why Dr. Tarlov limited his work to the cauda equina. It would seem to me that it might be possible to section any of the motor roots from the second to the twelfth thoracic and introduce a graft between the proximal and the distal end of any one of these thoracic roots. Examination of the nerve distal to the point of section, together with the muscle end plates, would then give much more definite information in regard to the actual amount of regeneration, because in the thoracic region there is no formation of plexuses and therefore the individual nerve passes out and innervates the segmental strip in its motor, sensory and sympathetic supply. No uncertainty is introduced by the possibility of an interweaving of fibers.

DR. THOMAS I. HOEN: I think Dr. Tarlov was disappointed that there was no functional recovery in these monkeys. The reason they did not use the limb may be that the part was anesthetic and the monkeys were not aware that there had been return of motor power. In this situation, monkeys differ somewhat from dogs in that the latter will continue to use the anesthetic extremity, owing probably to a more active mechanism for associative movements.

I should like to comment on Dr. Riley's suggestion that the intercostal nerves in the thoracic region be used. If one has worked with monkeys, one will realize that space is a factor to be considered and that the distance for work on a dorsal nerve root is very short. Even the cauda equina gives a very small space to work in.

DR. J. LAWRENCE POOL: I was very much concerned in the Army with the problem of paraplegia because so little could be done, both for complete transverse lesions of the cauda equina and for those of the spinal cord. That distressed me so much that I carried out an experimental study on a monkey, an attempt to bridge a gap in the spinal cord by anastomosing the ulnar with the femoral nerve. There was nerve regeneration along the femoral nerve after five months, so that movement was produced in that leg after the spinal cord was completely transected (Pool, J. L.: *Proc. Soc. Exper. Biol. & Med.* **62**:176-177,

1946). That is not an experiment comparable to Dr. Tarlov's work, for I allowed the spinal cord to remain intact until the nerve anastomosis had a chance to regenerate, so that the degree of muscular atrophy was not as marked as in his experiments. However, my procedure was somewhat encouraging. In this regard, a friend of mine talked to a German soldier, a paraplegic, on whom a surgeon in Vienna had tried the same thing (an ulnar-femoral nerve anastomosis) but there was no return of function. However, I think this type of procedure may lead to advances in the treatment of paraplegia.

I should like to ask Dr. Tarlov about one matter that I think deserves a trial (and I think he is the one to do it, because, so far as I know, he is the master of this particular technic of nerve suture), that is, the use of the sympathetic trunk or the splanchnic nerve as a by-passing measure. The autonomic pathways are often intact in a paraplegic patient despite transection of the spinal cord. If the splanchnic and sympathetic nerves are intact, why could not this technic be applied to these nerves in order to by-pass the transected spinal cord?

Dr. I. M. Tarlov: In answer to Dr. Stookey's question, I may say that we do have cross sections of the sciatic nerves from both sides. There was not a complete wiping out of all fibers on the side of operation, not at all; the degree of difference is approximately comparable to that in the longitudinal sections that were projected. It is not surprising that a considerable number of nerve fibers are intact on the side of operation, because the sensory ganglia are left intact; they are a source of the majority of nerve fibers. An accessory source might be the sympathetic nervous system, the postganglionic fibers. That question did not concern us a great deal, because the cross sections of the root proximal and distal to the graft showed beyond doubt that regeneration had occurred, and a considerable number of the fibers in the sciatic nerve must have come from the regenerated roots. Moreover, direct stimulation of the roots proximal to the grafts, which led to brisk contraction of the extremity, confirmed this view. The fiber counts on the sciatic nerve, of which we have done quite a number, have been greater on the side of operation than on the control side. That perplexed us for a while, but it is understandable in view of the fact that branching of the nerve fibers takes place at the site of suture, so that there is a plethora of nerve fibers in the regenerated nerve.

With regard to Dr. Riley's question, there must be some interweaving of fibers from the sympathetic system in the sciatic nerve, and some of the fibers in our preparations are doubtless of sympathetic origin. One could carry out the experiment Dr. Riley suggests: The intercostal nerves from the second to the twelfth thoracic segment are rather small, so that the question would be a little difficult technically, but not at all impossible. I did not do that because sections of the anterior roots at various levels distal to the grafts did show signs of unequivocal regeneration, as the electrical stimulation experiments had also demonstrated; but the experiments Dr. Riley suggests might be undertaken with profit.

With regard to Dr. Pool's interesting suggestion of anastomosis of a sympathetic trunk with the distal portion of the roots of the cauda equina, one certainly would get histological regeneration. The extent of the functional recovery which would be correlated with it would be difficult to foretell but it would probably be slight. If one did get regeneration, it is a question whether one would be successful in the matter of reeducating the patient to use the limb; I think the whole process of reeducation would be much simpler after a more direct approach, such as the use of nerve grafts between the stumps of the roots of the cauda equina.

Topectomy: A Surgical Procedure for the Treatment of Mental Illnesses. Dr. J. Lawrence Pool.

Topectomy is a form of cortical ablation which I developed, in conjunction with Dr. Robert G. Heath and Dr. John Weber, for the treatment of psychoses and other types of mental illnesses. It has been used instead of prefrontal lobotomy when psychotherapy, shock treatment and, in some cases, psychoanalytic therapy have failed. The operation consists of bilateral symmetrical excision of the cerebral cortex from the region believed to represent areas 9 and 10 of Brodmann in their rostromedial extent. At one stage a single frontal bone flap is reflected, the dura opened bilaterally and the cortex excised from the rostromedial aspect of each frontal lobe. Each excision is begun 2 to 2.5 cm. anterior to the

coronal suture at the midline. The block of cortex excised from each frontal lobe measures 5.5 cm. in the anteroposterior plane, 3.5 cm. in width and 2 cm. in depth.

There have been no operative fatalities in the 85 cases in which the procedure has been carried out thus far, and no permanent incontinence or paresis. The incidence of postoperative convulsive seizures has been 10 per cent, but seizures have always been controlled by anticonvulsant medication. There has been no appreciable deterioration of intellectual or emotional capacity as the result of this operation. The best results have been obtained in patients with obsessive-compulsive psychoses, all of whom are back at their preoperative occupations. The largest category of patients undergoing topectomy was the schizophrenic group, of whom slightly more than 50 per cent have so far maintained an excellent or satisfactory postoperative improvement. The maximal period of follow-up observations to date is 2½ years.

DISCUSSION

Dr. John Weber (by invitation): I shall try briefly to cover the psychiatric material. The following slide, prepared in October 1948 by Dr. Robert G. Heath, indicates the results obtained in 32 patients up to that time. Four of the patients on whom Dr. Pool and Dr. Heath operated as a pilot study are listed separately. On the remaining patients the operation was done after termination of the Columbia-Greystone project or while the Greystone project was in progress. All patients have been followed at least six months, and those in the original pilot group, up to 2½ years. At present, some 50 patients have been operated on, though not all have had a six months' follow-up study.

According to the numerical scale of improvement, 4 indicates that the patient is at home and functioning (working) at his old capacity, apparently as well as before his illness; 3, that the patient is at home, doing well and in some cases working, but not quite up to his preillness performance, even though he is capable of independent living; 2, that the patient is at home, under close supervision, or in the hospital on ground parole; 1, that the patient is still institutionalized, although more easily managed, and 0, that there is no improvement. All patients were institutionalized at the time of operation, or operation was resorted to in an attempt to forestall imminent hospitalization.

In the original pilot group, two patients did very well, and the other two made little improvement. Of the remaining 28 patients, nine achieved a top rating of 4 (seven with schizophrenia, one with an involutional psychosis and one with an obsessive-compulsive neurosis). Six patients achieved a rating of 3 (three with schizophrenia, one with a chronic agitated depression, one with a phobic neurosis and one with involutional paranoia). The remaining patients, who did less well, were chiefly schizophrenic, although one patient with a complicated obsessive psychosis, who had had a long period of psychoanalysis, and one psychopath were included among these patients who achieved a rating of 2 or less. The one psychopath was included with some trepidation, although there are theoretical reasons for expecting a good response to operation in some psychopaths. This woman now presents much less of a management problem; nevertheless, we do not yet recommend the operation for psychopaths. In summarizing the results, I may say that about 50 per cent of the patients have had a good or an excellent response. The majority of the patients were schizophrenic, and the larger number, both of failures and of successes, appeared in that group. The small number with depressions and obsessive psychoses have usually done well.

A word about the clinical course following topectomy: Usually there is a postoperative period of confusion and indolence. The patient may take a long time in the bathroom, and his behavior may be somewhat unpredictable; he may, as Dr. Pool has indicated, be incontinent of urine or feces for a time. This condition clears up in a period of time which varies considerably but is usually from two or three weeks to two months, the latter being the longest required for these more acute effects to disappear. A period of reorganization begins thereafter, which may last up to one year after operation.

In the Greystone series extensive psychological tests were carried out before and after operation, as well as clinical observations; so far as we have been able to determine clinically or from psychological testing, these patients show no consistent over-all loss of intelligence after topectomy. It is gratifying that they do not have the picture often reported with lobotomy, of being irresponsible or of having lost their ability to have warm relations with other people.

Psychiatrically, the effect of operation seems to be one of relieving effective or emotional pressure. This has been demonstrated by clinical observation, and the patients themselves, in their reports of what the operation has done, stress that they are able to relax, that they feel less tense, that they do not feel under pressure as they used to. They verbalize this in many ways, but it comes down to the same thing, that they are relieved of affective stress. In accordance with this, the patients with primarily affective disorders, patients with the involutional psychoses, patients with reactive depressions and patients operated on in the depressed phase of the manic-depressive psychoses have done well. We have now three patients with obsessive-compulsive neurosis, in whom, of course, the symptom is in response to a great deal of anxiety and constitutes a defense against the anxiety, and those persons, too, have done remarkably well, with loss of compulsions soon after operation. All of them had had long courses of psychotherapy, usually including unsuccessful psychoanalysis, and they had also had electric shock treatment, without responding to any of these procedures.

An interesting group, and the largest, is the schizophrenic one. The responses appear to be divided evenly between very good responses and poor ones, and a word about that is in order. I think that the effect of operation is the same in the schizophrenic patients as it is in the other patients, and when they do get relief it is on the basis of this diminution of affect, of emotional pressure. The problem appears to be one of how much the patient has in the way of resources, so that he is able to reintegrate, to reorganize, once this affective pressure has been relieved. Some of the schizophrenic patients who had made a good adjustment before they developed their illnesses have responded very well. Other patients, apparently those with a large genetic predisposition, or, to put it in another way, those who lacked ability to combat their illness, have not responded. Another point which deserves emphasis is that even when the schizophrenic patient does do well after operation he remains "schizoid" and the personality is very unlike that of the depressed patient or the neurotic patient, whose personality was better organized and whose symptoms were less diffuse before operation. When the schizophrenic patient does well, he makes a good adjustment in spite of his schizoid makeup.

In the selection of patients for the operation, we feel it is a good sign if the patient is still "fighting his illness" and still maintains a capacity for good emotional response. The patient who has been emotionally flattened by his illness does not seem to do as well. Another sign which may be of importance is that the patients who have a temporary good response to electric shock or insulin shock treatment also do well and seem to maintain improvement after topectomy.

From the psychiatric point of view, a great advantage of this type of procedure is that it is possible to carry out psychotherapy with these patients once they have got over the acute postoperative stage. It has been difficult to give psychotherapy to a patient who has had lobotomy, but with the topectomy patients it works well and does them a great deal of good. I feel it is an advantage to give psychotherapy, particularly if the patient is able to return to a good home environment—another factor which is of tremendous importance. If the patient gets good psychotherapy, it may make the difference between success and failure.

Dr. Foster Kennedy: I have not seen any of these patients since they were operated on, but I had the opportunity of sending one of the first to Dr. Pool for operation. His technic in the direction of improvement on the original idea of Egas Moniz, as well as his effort to make a physiologic approach, is to be welcomed. The mind has been treated too much as though it were an isolated entity, by verbalism; here we have a direct approach, which will be greatly improved, but, of course, not very quickly. It may take a generation before this direct approach, combined with the knowledge and use of electronics, will yield spectacular results. We are only on the threshold of great things, but tonight a foot has been put over the threshold.

Dr. Israel Strauss: A paper of this kind requires considerable time and exposition. To tell one only that the tense affect has been lessened is not enough. The psychiatrist unquestionably has at his command many details which, in a case of this kind, time does not permit him to present so that we can really appreciate what has been done, favorably or otherwise. For instance, one of the most difficult conditions to combat is the compulsive neurosis. Even the most optimistic psychoanalyst will tell you that this condition baffles him not infrequently,

and he keeps such a patient under treatment for a long time. Dr. Weber says his patients did improve; I should like to hear from him whether they lost their compulsions.

DR. JOHN WEBER: Yes, they did.

DR. ISRAEL STRAUSS: That is a tremendous step in advance in the treatment of that type of psychic disturbance. I recall that when Dr. Freeman first presented before this society, as he did elsewhere, the work that he and Watts were doing there was a great deal of skepticism. One could not find a psychiatrist who would recognize that operation as anything but a butchering process, but now there have been all sorts of modifications of lobotomy, and in some instances the surgeon reporting on the material has claimed that it is not only of benefit, but is somewhat superior to some other method. Freeman has again imported from Italy the ice pick method on the orbital plate, and he gets extremely good results with it, according to what he told me; I know a state hospital in which it is being used. Apparently, one fact is coming out of all this work—that is, that the mind can be influenced by some sort of operation, interfering somewhere with the functions of the anterior part of the frontal lobe. I do not think there is any question about that. The extent of that improvement varies, as has been well stated here, in different conditions and in different persons, depending, I think, not only on the section of the brain operated on but also, and largely, on the personality of the patient.

I had a schizophrenic patient, a woman who is now 35, and who was treated by Sakel with two courses of insulin treatment. He administered it himself. After each course the patient was apparently normal, at least socially adjusted, but she relapsed. Subsequently, about 100 electric shock treatments were given at different times, but finally the family consented to having Freeman and Watts do a lobotomy. The important thing is that, though the patient is even today in an institution, she has been out for three or four months at a time; she has been south to Miami, and to Atlantic City. Some of her delusions still persist, but they are not disturbing. However, out of a clear sky she might grab something and attack a nurse or a companion. This impulse passes very quickly. As Dr. Pool says, some of these patients do very well after operation, provided the environment in which they are placed afterward is favorable. This patient, unfortunately, has a mother who is psychotic, so that whenever she is sent home she has to go back to an institution after a short period. The lobotomy, however, has really made her much more socially adjusted. There is no question, as Dr. Kennedy said, that work of this kind brings out the possibility that one is dealing with a disturbance of the physiology of the brain, that one is not merely analyzing the functional side of the brain but is looking for something that is of material importance.

DR. I. S. WECHSLER: When frontal lobotomy was first introduced, both neurologists and neurophysiologists had a sense of discomfort, and even expressed aversion to the procedure. It was a blind therapeutic attempt. Not knowing what psychotic behavior is and what role the frontal lobe plays, one could not evaluate scientifically the effects of lobotomy. Furthermore, the concept of psychotic deterioration had to be revised. Obviously, there is nothing final about so-called deterioration, since the process frequently is reversible.

The fact is that clinically lobotomy has brought about in many instances changes in psychotic behavior frequently amounting to cure—this despite the fact that one did not actually know how the cure was brought about. Getting good results without knowing causes or understanding diseases is not a novel experience. Syphilis was successfully treated for centuries before it was known that there was a spirochete. Malaria was treated and cured with cinchona bark even though it was not known that there is a Plasmodium, that mosquitoes carry it and that there is an alkaloid in the cinchoma bark.

The importance of Dr. Pool's contribution, it seems to me, lies in the fact that he has introduced a more accurate method, which may lend itself to anatomic and physiological correlation. It is also a safer method in that one can avoid injury, particularly to blood vessels. I was glad to hear him say that the Brodmann scheme is not helpful. It always looked to me like a jigsaw puzzle. His statement, too, that the excised brain tissue which looked diseased was found to be normal on histological examination is very important. This means that the histological studies are too gross and are not capable of revealing pathological changes to account for pathological behavior. Until our methods become more refined, we

shall be unable to correlate pathologic changes with abnormal behavior. More refined methods, perhaps the use of isotopes, may throw light in the future. For the present, it is difficult for us to speak of psychological processes in physiological terms. Until we can, we must use psychological terms for abnormal behavior. The only tool at the disposal of the psychiatrist is language. This tool he uses effectively in evaluating psychological disturbances and in appraising recovery. In other words, language is both a diagnostic and a therapeutic tool.

DR. S. PHILIP GOODHART: Dr. Pool's informative presentation on a subject of such vital importance has indeed wide implications. An endeavor to correct a psychopathological condition by actual surgical approach is startling in its conception; although, of course, Dr. Pool makes no claim to originality in this wide field, his approach by specific operative procedure and his consideration of relations between structure and specific function bring us to much greater precision than the approach by less exact surgical methods—lobotomy, for example. It is indeed a definite step forward, and one that is most inspiring, to feel that personality itself can be influenced by attack on precise areas wherein lies the pathologic basis of man's behavior and conduct.

I am much impressed with Dr. Strauss's allusion to the patient with a compulsive neurosis. I have for some time been in a position to examine prisoners and to testify on behalf of the state in criminal cases. Singularly, in recent years it appears that many crimes have involved persons in whom startling abnormal sexual behavior has been a prominent feature, and in most of the cases that I have seen the outstanding factor has been that which one sees in the patient with a compulsive neurosis. These persons exhibit abnormalities of conduct and behavior found in the constitutional psychopath. Very few of them could be called insane, certainly according to the medicolegal conception. There is a notable similarity in the mental construction of persons showing sexual perversion, especially of the assaultive, sadistic type. Indeed, the intellect and general conduct of so many of these patients approach the normal in other relations that one is often amazed at their outstanding compulsive behavior. Now and then the lay suggestion is made that surgery of the brain might eliminate criminal tendencies. As a matter of fact, if structure and function can be so precisely demonstrated and determined, then, indeed, we have reason to hope that abnormal behavior in which certain personality traits may be due to structural dysfunction may thus be surgically influenced. It is to be hoped that eventually we shall be able to recognize the precise localization in the frontal lobes of fibers connecting these frontal areas with other cortical centers, and perhaps the basal ganglia, where emotional impulses are automatically responsive to higher, more intellectual control.

DR. KURT GOLDSTEIN: One is surprised by the successes reported by the authors and can only congratulate them. It is interesting that an effect can be achieved by topectomy similar to that by frontal lobotomy. The main problem is whether the neural and emotional changes in the form of deterioration which the operation brings about as undesirable by-products are slighter in topectomy than in frontal lobotomy. From what we heard, these changes were not outstanding. It would have been interesting if the investigators could have given a more detailed report of the results of the test examinations and the behavior of the patients in everyday life. Studies on patients with frontal lobotomy who appeared clinically and socially improved have shown that they are nevertheless definitely modified in their personality and impaired in that mental capacity I have called the abstract attitude, a change I have considered characteristic of lesions of the frontal lobe. These changes in personality are easily overlooked in the use of the so-called intelligence tests. With tests one can study the quantitative differences of intelligence between persons, but not so well the defect we are confronted with in these patients, which is of a qualitative character. This comes to the fore with the use of special tests. The same concerns the judgment of everyday behavior. Only a careful analysis of the latter, which may appear superficially undisturbed, reveals a change in the personality which may be of the greatest significance for the life of the patient. I assume that the authors have taken this point into consideration and that their omission of its discussion was for lack of time. Perhaps they will tell us a little more about it in closing. Whether a patient is more or less disturbed in this respect with the use of one or the other method of operation is of great significance. The method of choice would be the one which not only gives the best result in the elimination of symptoms, but produces the least damage of the abstract attitude.

DR. IRVING J. SANDS: When Freeman and Watts introduced the method of Egas Monitz into this country ten years or so ago, we looked at it with considerable apprehension. However, very favorable results have been obtained in a considerable number of instances. There were several modifications of this method, each of which, however, resulted in considerable damage to the brain, and not infrequently in death from cerebral hemorrhage. Moreover, the methods employed were really blind ones, and the surgeon was working more or less in the dark. I am sure that the majority of us are now acquainted with Freeman's innovation of the ice pick method. The procedure introduced by Dr. Pool and his associates at least gives dignity to the human brain. It goes much further than that. It is an operative procedure performed under strict asepsis, and a method that one can understand; one can see the human being treated as a sick person, rather than a piece of ice. Furthermore, the method introduced by Dr. Pool is certainly less hazardous and is an open one, so that every one can see and understand it. I am confident that at the current stage of psychiatric therapy his method will prove a boon to the large number of patients with chronic and serious mental illnesses—that large group which has been neglected, as described by Albert Deutsch in his recent book, "The Shame of the States." Dr. Pool's method is scientific and logical and is understandable by neurologists, psychiatrists and neurosurgeons; it offers a fertile soil for investigations in many aspects of neuroanatomy, neuropathology, neurophysiology and psychiatry.

I should like to ask what criteria the authors use in the selection of their cases with respect to the chronicity of the illness or the duration of the symptoms.

DR. THEODORE R. ROBIE: I was disappointed that Dr. Weber spoke as he did about the psychopaths. One of the most striking cases in which the operation was employed at Lyons, N. J.—and it was not a topectomy, but a lobotomy—was that of a homicidal psychopath, and I am with Dr. Goodhart in what he said about patients of that type. This man had seriously injured a number of attendants with true homicidal intent. Fortunately, none of them died, but one had a fractured skull, and a couple of others had broken arms. He has been an entirely passive person for the two years since the operation. In a presentation of lobotomy material at the hospital he sat on the platform all during the presentation by the physician, and everyone wondered who the quiet boy was. When the physician was ready to present the roentgenograms in the case, the boy patient brought them in and carried out the entire procedure quietly; afterward the audience was told that he was the homicidal patient who had carried on so wildly.

I do not think one can laugh off the ice pick operation. I have a letter from a friend in a state hospital on the West Coast who, after Freeman had visited the hospital, carried out a number of these operations, with surprisingly favorable results, so good that they were reported over the radio.

DR. LAWRENCE POOL: The first patient Dr. Kennedy sent me was the second one in our early series, operated on 2½ years ago. She had been confined to a state hospital for several years. She was admitted in a camisole and had to be maintained in this for several days until we could arrange for operation. Since topectomy she has been home, doing the cooking and shopping, holding also a part time job and occasionally taking her children by plane to Florida.

In connection with the personality factor Dr. Goldstein referred to, I think the whole question involves whether or not one should take the risk of a personality change by resorting to surgery. We do not think any of our patients were any worse off than they had been before operation, even those who did not get better. Of those who have gotten better, as Dr. Weber pointed out, about 25 per cent are really excellent so far as I can tell, while another 25 per cent may lack something in personality—perhaps what Rylander was getting at last year, that is, some are a little slow on the pickup, and some are slightly euphoric. This is a risk to be considered. However, our patients are those for whom operation is a last resort. Some have been psychoanalyzed, and almost all have received insulin and shock therapy, as well as psychotherapy; in a word, they have had practically everything that can be offered at present. After all this has failed, we see them. I think it is better to run the risk of a slight personality change and get such patients back home than to leave them behind bars in an institution because we are afraid of a personality change.

Dr. Wechsler made an interesting point concerning the function of the cortex, as brought up by these procedures. This phase of neurology is on the verge of a new era in that respect, for much laboratory work has been stimulated by this kind of work, and in certain laboratories

ablation and other experiments on animals apparently yield specific effects which depend on the area of the cortex operated on.

Finally, we are beginning to find that in such operations a mass, or quantitative, factor, as well as a focal factor, is operative.

DR. JOHN WEBER: In answer to Dr. Goodhart and Dr. Robie, who asked about psychopaths and sex offenders, I did not mean that we discourage any operation. We do not recommend topectomy because we have performed the operation in only one case and it would be an experimental procedure to employ it in others. I think affective tension is one of the basic factors in the individual case, and the degree to which the patient is under pressure is an important criterion in determining responsibility for his actions. The patients would have to be carefully selected and studied. It is something which should be done, but we have little experience with this problem.

I should like also to answer in part Dr. Goldstein's questions. A staff of psychologists did some 33 psychological tests on the Greystone patients before and after operation. They were careful to include the tests which Dr. Goldstein has indicated as being of value in evaluating function of the frontal lobe. All these tests showed no consistent diminution of the patient's ability to perform. As a matter of fact, many of the patients improved after operation in specific tests. That does not mean, I think, that the operation added something. It appears that with the relief of their illness their performance was improved. I agree with Dr. Goldstein that tests are not the answer to the problem. The changes are subtle and can best be picked up by observation of the psychiatrist or by members of the family, particularly the latter, since they see the patient more. We have been careful to get as much information on them as possible and have had, in general, favorable reports of improved emotional response. Probably the best way to test for that is in the neurotic patients, who are better preserved than psychotic patients. One of our patient's performances improved markedly after operation, after relief of his compulsions, and he was at least as good as he had ever been before. In addition, his wife commented that he was much more understanding and warm than before his illness. He had never displayed affection toward his children but was able to do so after operation. These are only straws in the wind to indicate the way we feel things are going.

In answer to Dr. Sands, we do not feel that a chronic illness in itself contraindicates operation. The more important factors seem to be the degree to which affect is preserved and plays a part in the illness, the degree of achievement and the basic personality, before the illness developed.

Choreoathetosis in a Case of Brain Tumor, with Surgical Treatment. By DR. JUAN NEGRIN JR. (by invitation).

No instance of juvenile choreoathetosis secondary to cerebral neoplasm is mentioned in the medical literature. A case of this condition dating from childhood in a patient with a neoplasm of the brain is accordingly presented.

A white man aged 20 had choreoathetoid movements of the extremities of the left side, with mild motor weakness, of 13 years' duration, and personality changes of four years' duration.

The family and past histories were noncontributory. For 13 years his local condition has not changed.

Roentgenograms of the skull, taken in September 1948, revealed a nodular calcific body to the right and posterior to the dorsum sellae. Roentgenograms of the skull taken at the onset of the present illness, 13 years previously, were reported as showing nothing abnormal, but a review of them demonstrated evidence of calcium deposits of a location similar to those in the roentgenogram of September 1948.

Pneumoencephalography showed no remarkable distortion of the ventricular system.

Through a right frontotemporal flap, by previous removal of cortical area 6, with extrapyramidal components to the arm and leg, the tumor was approached and its soft dome removed. The thalamus was displaced posteriorly and the lenticulostriate area laterally. Histopathological study revealed that the tumor was an astrocytoma. Three and a half months after uneventful postoperative recovery, the involuntary movements had not returned, but hemiparesis of mild degree was still present.

It is postulated that the tumor interrupted the suppressor circuit acting on extrapyramidal cortical centers, producing the release of their activity and resulting in the appearance of the choreoathetoid movements.

The fact that no return of involuntary movements has yet been observed may be due to the removal of cortical extrapyramidal areas and their cortical pathway, to the cessation of the pressure effect of the tumor on the subcortical suppressor circuit or to their combined action.

Lewis D. Stevenson, M.D., *President, New York Neurological Society, in the Chair*

Combined Meeting, Jan. 10, 1950

Compression of Spinal Cord Resulting from Bony Changes in the Spine Following Castration. DR. HAROLD MERWARTH and (by invitation) DR. ARNOLD DE VEER, Brooklyn.

Three cases were presented in which signs and symptoms of compression of the spinal cord followed castration for a malignant growth of the prostate gland. The compression was unusual in that it resulted from bony proliferation of the laminas and pedicles. Return of function of the spinal cord followed the laminectomy and removal of the bony overgrowth.

Spinal involvement from cancer of the prostate commonly results from vertebral collapse, extradural extension of the cancer tissue and, less rarely, root implantation. The three cases of overgrowth of the laminas and pedicles represent a phase of metastatic involvement of bone which is probably brought about by the increased longevity of the patient resulting from castration. Undoubtedly, this fortuitous occurrence will be observed oftener as patients have longer survival periods.

DISCUSSION

DR. E. JEFFERSON BROWDER, Brooklyn: I had the ill fortune to have operated on all three of these patients. Dr. Merwarth has brought to your attention something which we have not encountered before. As all of you are well aware, the usual means of disturbance of function of the cord by metastatic carcinoma is that of a collapsed vertebra or invasion of the spinal epidural space. This hypertrophy of the vertebral arch, however, is something we have not observed prior to the therapy that is now instituted for carcinoma of the prostate. I do not think one could designate this compression as either a clinical or a pathological entity. It does not seem to differ from other types of compression of the spinal cord that might result from metastatic carcinoma. It would appear, however, that a surgeon might be justified in subjecting the patient to a laminectomy in view of the fact that occasionally, as in one of the present cases, the patient may be rehabilitated. In the other two cases, as reported by Dr. Merwarth, the survival period after operation was short. Be this as it may, here is an unusual lesion occurring in the course of an old, well known process—something that we had not seen before, and Dr. Merwarth thought it should be brought to your attention.

Surgical Treatment of Intracerebral Hematomas. DR. E. JEFFERSON BROWDER and (by invitation) DR. EVERETT W. CORRADINI, Brooklyn.

During the past seven years we have had experience in 61 cases of intracerebral hematoma of varying pathogenesis. Thirty-two patients sustained head injuries, ranging from minor contusions of the scalp to compound fractures of the skull. In 11 patients arterial hypertension appeared to be the cause. Six patients had anomalies of cerebral blood vessels: One of these had an angioma of the left cerebral hemisphere; four had a single aneurysm of the anterior half of the circle of Willis, and the sixth had two saccular and three fusiform aneurysms of the circle of Willis. For the 12 remaining patients no satisfactory explanation of the intracerebral hemorrhage was found. We no longer make any practical distinction between intracerebral hematomas of traumatic origin and those of spontaneous origin. Rather, it has seemed more significant to classify them according to clinical features. The commonest, and most important, clinical sign observed in this study was alteration in the state of consciousness. On this basis the patients were divided into three groups. The first group consisted of 15 patients who lost consciousness at the onset of the illness and remained stuporous, with little or no improvement, until death: Nine had evidence of head injury; 4 had hypertensive vascular disease; 1 had an aneurysm, and in 1 the cause was obscure. Operation was carried out on 4, without improvement. The second group included 21 patients

who lost consciousness at the onset of illness but who showed definite spontaneous improvement thereafter: Fifteen of these had sustained head injuries; 2 had arterial hypertension; 1 had a cerebral angioma, and in 3 the cause of hemorrhage was unknown. After periods ranging from three days to three weeks, seven patients of this group who were not operated on deteriorated rapidly and died. Partial or complete evacuation of the hematoma was effected in 14 cases, with four deaths.

The third group consisted of 20 patients whose illnesses began, singly or in combination, with confusion, headache, speech disturbance or sudden weakness of the extremities of one side. Drowsiness followed by stupor did not appear for intervals ranging from 15 minutes to several days. Of the 20 patients, five had sustained trauma to the head, five had hypertensive vascular disease, three had aneurysms and the cause of hemorrhage in seven was obscure. Eight died without surgical intervention. Operation was performed on 12 patients, with six deaths. For five patients, historical data were so inadequate that classification was not feasible.

Localization of the hematoma was effected by aspiration of material from the suspected area through a ventricular cannula or by ventriculography, pneumoencephalography or arteriography. We believe that ventriculography is the procedure of choice.

Removal of the hematoma by aspiration through a ventricular cannula was performed in 15 cases, with a mortality of 73 per cent. In nine instances further operation or necropsy showed that this procedure had failed to remove solid clots of significant size. We have abandoned this method except as a palliative measure in occasional instances.

Complete removal of a collection of blood through a cortical excision was carried out in 19 cases, with a mortality of 31 per cent. In our opinion, this is the only adequate method of removing an intracerebral hematoma.

The over-all mortality rate for the 35 patients operated on was 51.4 per cent. Of the 17 who lived after operation, nine showed satisfactory improvement, and eight remained greatly or completely incapacitated by disturbances in motion or speech.

DISCUSSION

DR. LEWIS D. STEVENSON: It seems to me that any large hemorrhage into the brain is likely to be fatal unless some attempt is made to remove it. I do not think this subject has been discussed enough among members of this society or among others interested in the condition. I remember that 25 years ago Alfred Taylor used to try to tap these spontaneous intracerebral hemorrhages and sometimes was able to save the patient's life. Later, Dr. Penfield did the same thing, and so have others; now Dr. Browder and Dr. Corradini have brought the results of their experience with a very large material, and I shall be glad to hear what Dr. Browder has to say in the discussion of this problem. I should like to know whether most of this blood is clotted when one attempts to remove it, how much is clotted, how long it takes to clot and whether postmortem study of the brains was made after or before fixation with regard to the extent of the remaining blood clot.

DR. E. JEFFERSON BROWDER, Brooklyn: This is an old story, and one that you are all entirely familiar with from the pathological standpoint. To add a little to the statistical report which Dr. Corradini gave you, I should like to draw attention to the frequency with which we have found hemorrhages in the head in different locations. During the past 15 years we have had 30,350 craniocerebral injuries at the Kings County Hospital, and these did not occur simply among "drunks"—they were real head injuries. Among these were 514 verified subdural hematomas. At this institution approximately 80 per cent of all the "traumatic" material is autopsied; so while we may have missed a few subdural hematomas, I should say they were few. There were 514 subdural, 106 epidural and 112 intracerebral hemorrhages which we considered of surgical significance, that is, amounting to 25 Gm. or more. Many discussions and papers have been devoted to the old subject of epidural hemorrhage; yet intracerebral hemorrhage has received scant attention. Dr. Corradini included in the presentation a few cases of spontaneous hemorrhage. The 112 I mentioned were all considered to be the result of trauma. Many of these patients with large intracerebral collections of blood were not rehabilitated by surgical therapy. A sufficient number were rehabilitated, however, to warrant continuing of our efforts. If one looks at the report of Turney and myself in which the cases up to 1942 were reviewed (*New York State J. Med.* **42**:2230

[Dec. 1] 1942), one can readily see how we were skirmishing, trying first one method and then another. Few of the 80 patients in that series (29 were subjected to operation) were rehabilitated. In other words, a little progress is being made in the care of patients with this particular lesion.

As to the lesion itself, at necropsy we have encountered a great variety of physical states of the clot. I say "clot"—it should be called a collection. Some were entirely liquid, others were entirely solid; the majority were a mixture of the two. Many of the hematomas disclosed eight to 10 days after injury were solid clots; some, three to five days after injury were entirely liquid. Gradual liquefaction of a subdural collection does not always take place. Probably the same may be said of the collections in the intracerebral position.

There is one other feature relative to definitive diagnosis that I might mention, namely, the use of arteriography rather than of ventriculography. Arteriography has been used by us; however, we are much more familiar with the interpretation of the ventriculogram than of the arteriogram. Possibly that accounts for the frequency with which ventriculography was used in the series just reported by Dr. Corradini. I should like to hear a comment from Dr. Wechsler or Dr. Gross. They have perhaps had a larger experience with the results of arteriography in diagnosis of intracerebral clots than we have.

DR. I. S. WECHSLER: After hearing such a fine paper, including so many cases of traumatic hematoma, I hesitate to discuss it. At the Mount Sinai Hospital we see comparatively little traumatic material; our experience is limited to so-called medical cases. The two problems which confront us are the differential diagnosis of intracerebral hemorrhage or thrombosis and tumor, and tumor and spontaneous hemorrhage or hematoma. Our interest in arteriography extends to the differentiation of such conditions. Air studies are valuable, of course, especially for localization; but by means of arteriography we can better differentiate between hemorrhage and thrombosis. The arteriogram shows cutting off of the arterial tree in thrombosis and a splotchy spread in hemorrhage. In hematoma the vessel—for instance, the middle cerebral artery—may be pushed aside, elevated or depressed. The arteriogram is all the more important as frequently the history alone does not indicate whether the lesion is a vascular one, a hemorrhage into the substance of the brain or a tumor. All know that the advent of a glioma may be so rapid as to simulate a hemorrhage and that a hematoma may develop comparatively slowly. Only recently, we had at the Mount Sinai Hospital three patients with intracerebral hemorrhage, all of whom were admitted with the diagnosis of brain tumor. All three were operated on and the hematomas evacuated; two are living and one died.

It is our opinion that arteriography is to be considered in every case in which intracerebral hemorrhage or hematoma is suspected if the general condition at all warrants it. In our experience, the few good results obtained were in patients below 50 years of age, in whom general cerebral arteriosclerosis is not likely to be present. I shall mention only one or two cases previously reported. A woman writer of 39 had onset of hemiplegia, aphasia, homonymous hemianopsia and a hemisensory syndrome. For some reason, she was kept at home for 48 hours without medical treatment. She had no hypertension. At operation fluid blood was evacuated. Almost immediately she could lift her right arm and say a few words. To make a happy story short, she walked out of the hospital, and her aphasia cleared up to the extent that she subsequently went back to her literary work. Another patient with complete aphasia and hemiplegia had a blood clot removed and began to recover speech and power the next day. So far the number of patients showing recovery is small, but if only one in five, or even ten, with cerebral hemorrhage can be helped the percentage is not too small. I agree with Dr. Browder that exposing the brain to evacuate the hematoma is better than blindly and incompletely evacuating it by means of a cannula.

DR. LEWIS D. STEVENSON: Dr. Wechsler, how do you differentiate between a thrombosed vessel and a hemorrhage like this by means of arteriography?

DR. I. S. WECHSLER (drawing on board): Here is the carotid artery, here the anterior and middle cerebral arteries and here the sylvian vessels. In thrombosis the contrast medium stops at the point of thrombosis, and the normal vascular arborization beyond is not visualized.

DR. LEWIS D. STEVENSON: How about hemorrhage?

DR. I. S. WECHSLER: The arteriogram in cases of hemorrhage is comparable in some measure to that seen with tumors. The vessels are broken up and merge into the hemorrhagic

area. More important, the hematoma pushes the larger vessels aside or elevates or depresses them. The arteriogram is not infallible. One needs long experience, and even then errors are possible. Sometimes a diagnosis of thrombosis is made when there is none, the error deriving probably from a spasm of the blood vesssel which cuts off the current. A second arteriogram may show patency of the arteries.

DR. IRA COHEN: I cannot add to what has been said, except to say that the large series presented by Dr. Browder and Dr. Corradini should give comfort to other neurosurgeons because what they say, on the basis of a group of cases such as this, must be authoritative. I can draw a valuable lesson from their division of cases. In other words, there is a group of patients for whom nothing can be done; there is a group for whom perhaps nothing should be done, and there is a group for whom something can be done and a good result obtained. The other lesson which we as neurosurgeons should learn from this presentation is that in many instances, perhaps not in all, better results will be obtained by excavation than by inserting a needle and guessing as to what is removed and what remains. The one objection I might see to excavation would be in a case of hemorrhage on the left side in a speech area, in which the question would arise whether more harm would be done by incision and turning out a clot than by an attempt to improve the patient by simple aspiration.

DR. ABRAHAM KAPLAN: The most important question is to determine which patients fall into the third group—in other words, which patients will benefit from surgical intervention. If we could select these patients, our results would, of course, improve. In October 1935 I presented before this society two cases of cerebral apoplexy in which I operated, with recovery in both. I followed one patient ten years, during which period she was perfectly well and then I lost track of her. The other patient I have followed up to date, and a fortnight ago I received from her a Christmas card telling me she was perfectly well. When I first examined this patient, she was in coma and had left hemiplegia. Because of chronic otitis media on the right, I suspected an abscess of the temporal lobe; on exploration I found an intracranial hematoma, which I aspirated, and she recovered completely except for partial left homonymous hemianopsia.

In the past year and a half, I have operated on three patients with intracerebral hematoma. One was at the Mount Sinai Hospital, where, in doing a ventriculographic study, I found an intracranial hematoma in the right postparietal region and evacuated it. The patient recovered completely except for left homonymous hemianopsia. He has remained well and is able to work. Another patient, who came under my care at Mount Vernon Hospital, presented the classic picture of spontaneous arachnoid hemorrhage. She was in coma with left hemiparesis. Subsequent air studies showed a displacing lesion in the right frontal lobe, and through a trephine hole an intracerebral hematoma was evacuated. She recovered fully and walked out of the hospital. In the last patient the hematoma was of traumatic origin. This patient, aged 28, came to the emergency room on a Saturady night with a small laceration of the scalp in the left temporal region, sustained during an altercation. The wound was sutured, and he was sent home. Three days later he was admitted to the hospital in a drowsy state with right hemiparesis and total aphasia. He gradually became comatose; at operation an intracerebral hematoma was found in the left temporal lobe, and this was evacuated. The man recovered except for alexia, some agraphia and nominal aphasia.

These five cases of intracerebral hematoma which have come under my care illustrate that selection of patients for operation, as was pointed out by the authors, will lead to a higher percentage of good results.

DR. WILLIAM EHRLICH, Newark, N. J.: The only surgical experience that I have had with intracerebral hematoma has been in cases in which I operated because I suspected a subdural or an epidural hematoma. In these cases my exposure was with the usual enlarged burr opening, and the hematoma was found by cannula exploration. In these cases the clot was evacuated by transcortical incision. The patients have all shown lucid or latent intervals in their state of impaired consciousness; I am impressed with the fact that, in the presentation of the evening, it was in the group of patients of this type that the best results were obtained. I have not operated in cases in which the initial cerebral accident has been so overwhelming that the patient remains comatose, with no fluctuation in his state of consciousness.

DR. HERBERT PARSONS: I should like to know what time the authors think is the best in which to operate for hematoma—whether they think there is much to be gained by waiting several days, provided the patient's condition will permit it; whether they think smaller associated hematomas may clear and the edema subside around the hematoma, and whether it is easier to evacuate the hematoma if a period elapses before removal is attempted, or whether one should make an effort to attack it earlier. I should like also to ask the authors how often, when they thought they were dealing with a hematoma, they have found an associated tumor with a hematoma around it.

DR. ARTHUR DALE CONSOLE: My experience with these lesions has been limited and does not compare with the series Dr. Browder and Dr. Corradini have discussed. I am amazed at the frequency with which they have seen these lesions. I was interested in Dr. Browder's suggestion that parenchymal hematoma is even commoner after trauma than epidural hemorrhage. I wonder whether I am missing them or whether they are not in my material.

DR. CARLOS G. DE GUTIERREZ-MAHONEY: One might point out that the incidence of intracerebral hemorrhage in Dr. Browder's cases of traumatic head injuries is only 1:300; I do not think that Dr. Console should be concerned about not encountering these lesions when in over 30,000 cases Dr. Browder has seen only 100. Few see 300 severe head injuries a year; if so, we might expect to see one traumatic intracerebral hematoma a year. I am always surprised, when cutting the brains of persons who have died of intracerebral hemorrhage, to note the extensive degree of damage of brain substance, extending not only into the hemispheres but also into the brain stem; with such a lesion, it is scarcely possible to anticipate a favorable result.

I am also impressed by Dr. Corradini's case of the difficult nursing problem and custodial care for so long, with the sudden death. My colleagues and I have had similar experiences with such patients, especially those with hypertensive vascular disease; they present a discouraging problem, especially to the nurses; it is only by recapitulation and a critical analysis of such material that we shall be able to deal with the problems these patients present.

DR. LEWIS D. STEVENSON: I should like to say that these secondary hemorrhages in the brain stem are the result of the tremendous pressure above—hence the advantage of recognizing the condition and operating for it before the condition occurs; I believe that they are not primary, but purely secondary, and must take some time to occur after the pressure in the brain has become very great.

DR. FRANCIS A. ECHLIN: I may mention two patients I recall at Bellevue Hospital who, in the initial stages, presented a picture suggesting a subdural hematoma following trauma. The patients gradually became symptom free, with a normal neurological status. They were up and around the ward, but because they had presented a picture of hematoma in the early stages, we obtained an encephalogram. In each case this showed a large intracerebral hematoma, for which we operated. In other words, patients may suffer with chronic intracerebral hematoma, as well as chronic subdural hematoma.

DR. JUAN NEGRIN JR.: Although I have been subject to Dr. Browder's teachings for some time, I still marvel at his experience and his excellent work. Some here agree that a number of intracerebral hematomas are better diagnosed by ventriculography, and others feel that arteriography should be used; I should like to ask Dr. Browder what he thinks about using a combined method, that is, ventriculography and arteriography. In ventriculography the appearance of the ventricles determines the location of the mass, but the cause of this hematoma may be overlooked because a superficial hemangioma or an aneurysm might not be in relation with the intracranial hematoma they caused and would be missed with ventriculography alone. This is why I should like the opinion of Dr. Browder and Dr. Corradini on the use of the combined method. Another question is: When a hemangioma or an aneurysm is the etiological factor of an intracerebral hematoma what should be done after the removal of the hematoma? Is it not reasonable to treat the other lesions?

DR. S. PHILIP GOODHART: The excellent and informative paper by Dr. Browder and Dr. Corradini has given us a wealth of material on a subject that becomes a matter of deep concern to every neuropsychiatrist and neurosurgeon. The pathologic process that immediately follows and subsequently changes remains obscure. Bleeding into cerebral tissue, at first

minute and finally becoming what might truly be called intracerebral hematoma, makes immediate differential diagnosis from other conditions, such as neoplasm, most difficult; the clinical progress of these vascular conditions keeps the physician in a state of anxiety.

In my experience, immediate unconsciousness has been the earliest clinical sign. The profound disturbance in consciousness is perhaps a point of differentiation. I feel it may even be one of the pathognomonic signs in differential diagnosis. My experience has been that even minute intracerebral bleeding may produce profound unconsciousness. I am impressed with the slight fluctuation in the progression of symptoms often shown in these cases. I refer not to the not uncommon cases of hemorrhage into the internal capsule or of direct or indirect ventricular hemorrhage or leakage but to small vascular leaks, including those that may have origin in deep-seated aneurysms. The approach suggested in the masterly presentation this evening impressed me as an important contribution to neurosurgery.

DR. EVERETT W. CORRADINI: The proper time to institute surgical treatment of an intracerebral hematoma depends on the clinical features of the individual case. We are predominantly influenced by the state of consciousness. Patients in the first group who remained profoundly stuporous seemed to benefit little from operation. When patients in the second or third groups did not recover completely or regressed after partial improvement, the institution of definitive therapy was indicated.

Sometimes the clinical manifestations of an intracerebral hematoma mimic or obscure the signs or symptoms of a subdural or an extradural hematoma. Therefore the diagnostic procedure of ventriculography is used to reveal not only the intracerebral collection but also other space-occupying lesions that may exist in other locations within the cranium.

Hemorrhages in tumors have been excluded from this study. We have had two cases of what was diagnosed and treated as intracerebral hematoma in which the collection was found to lie within a glioma.

We are a bit hesitant about performing pneumoencephalography in the presence of a space-occupying lesion. We feel that ventriculography gives a greater margin of safety. In the average case, the use of combined arteriography and ventriculography is perhaps superfluous. Either method seems adequate in itself if properly performed.

The treatment of aneurysms and angiomas is a function of the accessibility of the lesion and the condition of the patient. If possible, we believe such lesions should be removed.

Cases of Abortive Schizophrenia. DR. WILLIAM MAYER.

For more than 10 years the author observed a group of patients with certain distinct basic schizophrenic symptoms, such as an inclination to autistic thinking, inclination to withdraw, feelings of depersonalization, feelings of unreality and superimposed neurotic, mostly compulsive, features. Such persons never become psychotic; they do not have to be hospitalized; they work, have some insight and never deteriorate emotionally or intellectually. They form a distinct unit, and their condition is quite different from the so-called pseudoneurotic forms of schizophrenia. They show that current ideas of what schizophrenia is must be changed and that the concept of schizophrenia must include not only the classic forms, but various milder forms. In 85 per cent of the cases there is a distinct hereditary pattern, with affective and schizophrenic disorders in the ancestry. The presence of affective disorders in one part of the ancestry is probably the reason that the disease never becomes severe. The study of these patients not only is of great clinical interest, but helps one to have a better idea of the prognosis for the psychoses.

DISCUSSION

DR. PAUL H. HOCH: In the last few years my colleagues and I have devoted considerable time to studying patients of this type. As Dr. Mayer stated, at the beginning there was noticeable a certain resistance to the broader concept of schizophrenia. A large number of patients who were formerly called neurotic are now classified as schizophrenic. Actually, follow-up studies show that this diagnostic approach is justified, for many of these patients, by and large, later have a schizophrenic pyschoses. Theirs is the condition known as the pseudoneurotic form of schizophrenia. This designation is used for the reason that many of these patients are, unfortunately, classified and treated as neurotic. The diagnosis of schizophrenia must be employed differently today than it was 30 or 40 years ago. Among the

full-fledged forms of schizophrenia, not the attenuated ones, one finds the classic four types: simple, paranoid, hebephrenic and catatonic; but these do not cover the symptoms of all patients.

Today one distinguishes the so-called acute confusional schizophrenia, the schizoid hysterical reaction, the periodic, or cyclic, forms of schizophrenia and the symptomatic schizophrenias. I wish to mention this array of subgroupings, which is now fairly well marked, in order to indicate that these forms of schizophrenia have different nosological backgrounds and different prognoses; they respond to various treatments differently; therefore a knowledge of these forms is important.

I agree with Dr. Mayer's statement that practically no textbook of psychiatry contains a description of patients who are in the first phase of the schizophrenic psychoses. There are usually descriptions of patients in whom the mechanisms of defense and disorganization are already in full action, and therefore the picture is not that which one sees in the attenuated, or early, forms of schizophrenia. To mention one point, anxiety is never mentioned as a prominent feature; even so, it is probably one of the most important symptoms.

We have material on over 300 patients, with the so-called abortive forms of schizophrenia, and those 300 patients fall roughly into two groups. The first is the so-called schizoid type, originally defined by Bleuler and later described in detail by Kretschmer and others as rather peculiar, egocentric persons, considered by others in the community as odd; many of them are highly intelligent and very capable, but there is an impairment in their social relationships. These patients, interestingly, do not show any subjective symptoms. They usually do not complain of symptoms. They remind one of the picture of a character neurosis; actually, the patient believes he is normal; his associates, however, state that he does not function quite right, especially in the social sense. This group is a large one, and one sees a number of such persons among the relatives of schizophrenic patients.

The second group is one I described as the pseudoneurotic group, usually showing symptoms of a neurotic type, with a peculiar anxiety makeup designated as pananxiety and a peculiar sexual structure designated as a chaotic sexual structure. One also sees the interesting phenomenon of anhedonia and many other clinical symptoms, which we described in our paper. Dr. Mayer's cases actually do not differ from ours, for the subjective symptoms of all these patients there are depersonalization, hypersensitivity, peculiar hypochondriacal complaints and anxiety. He probably described them as somewhat different from ours because his patients did not exhibit any psychotic episodes. Many of our patients did not show them either.

I should like to discuss briefly the genetic factor. In his case material he demonstrated that usually one parent has schizophrenia or a schizoid emotional organization, whereas the other parent has an affective disorder. This was interesting to me, because our material does not confirm that statement. Only a comparatively small number of our patients show this genetic relation. We have many patients whose parents are schizoid, and we have patients with a brother or sister who has a full-blown schizophrenia, but this particular combination Dr. Mayer has described we have seen in only a very small number of patients, and I do not know what significance we may attach to Dr. Mayer's figures. I do not understand how he found so many patients with this particular genetic combination.

Dr. Mayer mentioned that manic-depressive components in these patients attenuated the psychosis. This hypothesis has been put forward several times by many psychiatrists, who have stated that this manic-depressive component probably helps to prevent deterioration in the patient. More attention will have to be paid to this observation in the future in order to determine its validity. I wish to call attention to a group of patients whose illness starts with manic-depressive symptoms, later becomes increasingly schizophrenic and finally presents a typical picture of schizophrenia. In such cases the manic-depressive component is of no help.

The prognostic evaluation of these patients is interesting. They fall roughly into three groups. The first group remains as Dr. Mayer's cases indicate, about the same, or under the influence of psychotherapy shows some improvement. A psychotic episode does not develop, and the patients do not deteriorate. The second group shows the pseudoneurotic or abortive symptomatology, and very often, under the influence of physical or mental stress, psychotic

episodes develop. These episodes sometimes last only a few days, and then the patient recovers. In the third group there slowly and progressively develops a full-fledged schizophrenic picture.

It is this group of patients which is most difficult to treat. It is much easier to treat a patient with overt schizophrenia than these patients. Dr. Mayer has already mentioned that they do not respond to shock treatment. In some patients shock treatment may even light up the psychosis, if it is not carried out judiciously. In reaction to shock they behave like neurotic patients, whose response is not lasting.

About 20 per cent of these patients respond to psychotherapy; however, it has to be carried out quite differently than it usually is. These patients constitute the largest number of analytic failures. Orthodox psychoanalysis is not the treatment for these patients. Usually they need a much greater ego support under treatment than do neurotic patients. Definite instructions on how to handle life situations must be given much more thoroughly than in the analysis of the neurotic patient. There are many other features in the analysis of these patients, which I shall not discuss for want of time. I wish to emphasize that the patient needs psychotherapy which uses some analytic interpretation, but the basic need is the ego support and the attempt to unravel his social relationship to others. A new treatment was introduced for these patients a short time ago—topectomy. I shall not discuss this in detail, for I shall soon have the privilege of presenting material treated by this particular approach; suffice it to say that quite a number of patients who did not respond to psychotherapy or any other approach were treated by topectomy, with remarkable results. It is not a treatment which will help all patients with abortive schizophrenia, but a surprising change in their social relations occurs in many of these patients after topectomy.

Dr. Lothar B. Kalinowsky: It should be stressed that these cases have an enormous importance for the psychiatrist working outside mental hospitals. Dr. Hoch, in his first description of this group, and Dr. Mayer, in his representation, pointed out what a difficult diagnostic problem these cases of schizophrenia present. The treatment is far less satisfactory than that of full-fledged psychoses of the schizophrenic group. Shock treatment is usually unsuccessful. A number of these patients are among those voluntarily admitted to the Psychiatric Institute, where many of them have been given electric shock therapy, without convincing results. In some an acute psychotic syndrome has developed under electric shock treatment. This was first taken as an activation of the schizophrenic disease, but it was later recognized in most cases as a symptomatic organic psychosis, which cleared up in less than a week but did not lead to improvement of the original disease, as had been hoped. Insulin treatment may relieve some of the tension of these patients, but it does not lead to any more lasting effects than electric shock therapy. Psychotherapy is also not too promising, as was pointed out, although it may keep the patient functioning on some level for a considerable length of time. By far the best treatment for the group is psychosurgery, and some of the best results I have seen with psychosurgery have been in cases of this kind. It is true that the hereditary background which Dr. Mayer stresed often makes one alert in looking for schizophrenic features in a patient with primarily psychoneurotic symptoms, although a history of affective episodes in one of the patient's parents could easily refer to a case in which the condition later turned out to be schizophrenia of episodic character. The diagnosis will have to be made from the symptoms. The psychosurgical procedures will probably be considered even earlier in the future, when neurosurgeons have better learned to apply more refined procedures than lobotomy; but even with standard lobotomy excellent results have been obtained in these patients, with fewer side effects than in any other schizophrenic group.

Dr. William Mayer: I wish to thank Dr. Hoch for his interesting comments; he has a larger experience than I have. I separated my cases from the so-called pseudoneurotic group, first, because none of my patients had psychotic episodes and, second, because the genetic aspect in my cases was different from those he described.

To Dr. Kalinowsky, I wish only to say that in the series of patients with affective disorders I have seen most of the mothers and fathers, and there is no doubt that one parent had not a distorted psychosis, but a real affective disorder. Twenty-five cases are not enough to justify one's drawing conclusions.

PHILADELPHIA PSYCHIATRIC SOCIETY

Robert S. Bookhammer, *President, in the Chair*

Regular Meeting, March 11, 1949

Effect of "Malononitrile" on Physical and Mental Status of Schizophrenic Patients. DRS. DIXON MEYERS, THOMAS E. SHOEMAKER, WILLIAM C. ADAMSON and LOUIS SUSSMAN.

This paper was published in full in the April issue of the ARCHIVES, page 586.

DISCUSSION

DR. PER-OLOF THURMAN: The question is whether mental disorders are somehow correlated with the nucleoprotein production of the cell and whether a change in the cellular metabolism will change the course of the disease.

The answer the Swedish investigators have given is positive. They base their opinion on the fact that they have found disturbances of the protein metabolism in psychotic patients, as compared with their results in other, reputedly normal persons. They base their opinion also on the fact that "malononitrile" was known previously to change the protein contents of the nerve cell and will change the nucleoprotein metabolism in experimental rabbits. The results of these experiments have now been applied in extended and repeated investigations and have given further valuable data. However, the question comes to mind of how well founded is the assumption of abnormal protein metabolism in connection with mental disorders.

I agree with Dr. Meyers and his co-workers that further large scale investigations are necessary. They confess that their evidence is based on four known cases, which cannot be regarded as sufficient, as they also point out. I shall not discuss the biochemistry, however interesting. I have in mind a question on which I should like to have Dr. Meyers' opinion. It is known that insulin also increases the protein content of nerve cells. "Malononitrile" is more agreeable to the patient than insulin. "Malononitrile" undoubtedly increases the protein content of the nerve cell; insulin does this also. I wonder whether there is a link, and whether Dr. Meyers thinks his experience with "malononitrile" actually supports the idea of replacing insulin in certain cases with "malononitrile."

DR. DIXON MEYERS: With regard to the question of "malononitrile" replacing insulin, at present I do not think one could say that it should. It is true that in some of these cases "malononitrile" did as much as has insulin in the past, but the drug is still too new to be considered a substitute.

Pseudocyesis: A Clinical Endocrine Study. DR. PAUL H. FRIED and DR. A. E. RAKOFF.

In a study on 24 women with pseudocyesis, constituting the largest single group to be reported to date, the clinical manifestations were correlated with the endocrine and psychiatric findings. The usual symptoms and signs of "pregnancy" were sufficiently evident to convince 16 (40 per cent) of the examining physicians on the initial examination that eight (33 per cent) of the patients were pregnant. Absence or diminution of the menstrual flow, abdominal distention, swelling and secretion of the breasts and the presence of "fetal movements" were present in almost all cases and had convinced the patients that they were pregnant.

By means of hormonal assays of the urine and endometrial biopsies, it was possible to establish the following endocrine pattern as the mechanism of disturbed function. Such women apparently have persistent function of the corpus luteum, as indicated by significant amounts of estrogens in the urine on assay and varying degrees of secretory (progesterone) activity in the endometrium, as shown by biopsy. Furthermore, this persistence appears to be the result of stimulation of the ovary by lactogenic hormone (prolactin, luteotrophin), as indicated by its presence in the urine of the four patients tested. These findings account for the "hyperhormonal" amenorrhea or hypomenorrhea and the clinical evidences of hyperestrogenism, that is, the changes in the breasts and uterus. It seems that the endocrine changes have resulted from psychical factors, which probably utilize pathways from the cortex through the hypothalamus to the anterior lobe of the pituitary, causing release of the luteotrophin and suppression

of gonadotropins. The psychogenic factor, a desire for pregnancy in a group of patients with sterility whose basic personalities were abnormal because of lifelong factors, directly produced the symptoms.

Endocrine therapy alone was not effective but was of value when used in conjunction with psychotherapy, which was the only effective means of treatment. Pregnancy resulted in four of the patients with previous sterility of two to seven years' duration.

From this study the following psychological mechanisms appear basic: An unconscious instinctual wish for maternity is fortified by environmental situations and tempered by early associations until, in predisposed personalities, pseudocyesis results. In this series, such "pregnancies" would have (1) secured faltering marriage, in seven cases; (2) proved the patient's ability to conceive and to become a complete woman, in four cases; (3) achieved parity with other women, especially close friends, in four cases; (4) obtained a child as an immature plaything and companion, in four cases; (5) effected self punishment to appease guilt feelings arising from aggressive impulses, in two cases, and (6) denied a fear of pregnancy, in one case. These postulates are quite in accord with earlier works of Paddock, Deutsch and others.

Pseudocyesis: A Psychiatric Study. Dr. Albert J. Kaplan and Dr. Robert Schobpach.

Nine women with pseudocyesis were studied psychiatrically. All were married; seven were Negroid, four had had chronic pelvic inflammatory disease and at least three had had previous pseudocyetic episodes. The basic psychological mechanism appeared to be a strong unconscious maternal instinct, fortified by environmental situations and tempered by early associations. Brief superficial psychotherapy was attempted with four patients and combined with other therapies with three other patients while the remaining two patients were interviewed only. Interview was unsuccessful, but only one of the other patients failed to respond. This suggests that pseudocyesis is probably more closely related to "hysterical" conditions than to deeper, more persistent psychosomatic disturbances.

It is interesting to note that all these patients were married and living with their husbands at the time of onset of the condition, whereas other reports have stressed its occurrence in the unmarried. All the patients were considered neurotic—two to a severe degree, and two others were still playing with dolls. The loss of both parents during childhood by four patients may account for some of the insecurity, which was prominent in all cases. Three patients had a marked degree of mental deficiency, as measured by the Kent Emergency Test; three had about dull normal intelligence, and three had normal intelligence or above. Contrary to previous studies, the incidence among Negroes was considerably higher than that among white persons (7 : 2), but this approximates the ratio seen in the gynecologic ward.

The high incidence of pelvic inflammatory disease (in 4 of 9 women) is considered significant in that it may serve to focus the libido on the uterus and, at the same time, to accentuate the need to prove fertility as the expression of complete femininity. Four patients had had previous "pregnancies" ending in three month "spontaneous abortions," but in only one was this substantiated by a fetus; the others produced only small blood clots. In addition to these possible pseudocyeses, three had had previous pseudocyeses—one, three—yet they were just as certain of being pregnant as the others.

DISCUSSION ON PAPERS ON PSEUDOCYESIS

Dr. Robert A. Matthews: Dr. Rakoff has been seeing an unusually large number of patients with pseudocyesis in the maternity outpatient department. In the past, the average had been about two patients per year, and in 1940 he had treated 14 patients with the syndrome. He thought it might be interesting to study them from a psychiatric standpoint. Two of the 14 reported. These two were not thoroughly studied, but they laid the groundwork for an interest in the problem, which was taken up by Dr. Rakoff, Dr. Fried, Dr. Kaplan and Dr. Schobpach. This study of 24 patients has been the result. As they mentioned, this is the largest series of patients studied by any group of workers to date. A series of 444 cases was discussed by Bevins, but these were collected from the literature. Bevins found pseudocyesis in children as young as 7 years and in a woman of 79. This group confined itself to a more natural age. I recall seeing a woman of 53, though I doubt whether she was a member of this series, in a ward at Jefferson Medical College Hospital several years ago; she was pregnant in a pseudocyetic way because of fear of losing her lover of many years.

The physical and mental examinations performed were so well described by the writers of this paper that there is little left for me to say. One comment might be in regard to the doctors who examined these patients. Perhaps it was a wish fulfilment to have these women pregnant which led these physicians to become careless in their diagnosis.

It is interesting that more than one physician erred in these cases.

DR. PAUL H. FRIED: It was not difficult to be fooled by these patients. Given a false positive Friedman reaction, it is difficult to convince oneself that a woman is not pregnant. Some have a greatly distended abdomen. Just why gas formation can occur and remain constant is difficult to understand; furthermore, its presence would not account for such a degree of abdominal distention. In this group the desire for pregnancy seemed to be the important thing. The illness was likened by Dr. Schobpach to a hysterical syndrome; however, we are not concerned with cases in which conversion phenomena are largely involved, since something in addition must be present in this group of patients. It certainly emphasizes the power of the psyche in influencing the endocrine system. Endocrine dysfunction can result from psychical influences. I do not think there is anything else I can add.

DR. A. E. RAKOFF: From the standpoint of the endocrinologist, this study is an illustration of another mechanism by which functional menstrual disorders on a psychogenic basis can be produced. From a physiological standpoint, there are three mechanisms by which psychogenic amenorrhea can occur. In the normal cycle the pituitary stimulates the ovary, which, in turn, produces the hormones which build the endometrium. There is good clinical evidence that this whole sex-endocrine mechanism is an extremely labile one, which is readily influenced by environmental factors and psychical trauma. In one group of patients the pituitary factor may be "knocked out." The gonadotropins disappear, so that there is no stimulation of the ovary. In some patients in whom the psychical trauma may be severe and affect other hormones of the pituitary gland a syndrome of anorexia nervosa, simulating Simmond's disease, could be produced. In still another group the pituitary gland may remain intact but the ovary may be "knocked out." Here, there is a normal pituitary, but the ovary is incapable of responding, producing a menopausal syndrome in young women. It is difficult to state which kind of trauma will produce which kind of response.

There is still another mechanism which may occur in patients with a fear of or desire for pregnancy. The gonadotropins are then blocked by another hormone coming from the pituitary, namely, the lactogenic hormone. So much of this coming from the pituitary blocks the other hormones that postpartum lactating women, for example, are usually infertile. The lactogenic hormone stimulates the corpus luteum and stimulates the production or increases the amount of estrogen and progesterone. This is a hyperhormonal amenorrhea, whereas in the other group of patients the amenorrhea was hypohormonal.

DR. SAMUEL A. ZERITSKY: It would be interesting if one could have more light on the way in which enlargement of the abdomen occurs. Were any roentgenograms taken of these patients' abdomens? Were any of the patients given total anesthesia? In some cases the enlarged abdomen relaxes completely under anesthesia. Were any drugs which affect the smooth muscle structures tried on these patients?

This phenomenon is apparently not limited to human beings; cases have been reported of pseudocyesis occurring in animals, usually after situations of a frightening nature.

DR. PAUL H. FRIED: With regard to the statement about urinary retention, we did not have any in which this was a factor; the distention in our cases persisted for periods ranging from four to 14 months. Biven noted this type in his group.

With respect to cases of distended abdomen in which distention of the intestine was shown in the roentgenogram, we had three patients who revealed rather interesting findings in this regard. When one of these patients was lying on the table in the gynecologic clinic, the abdomen would tend to relax. On arising, her abdomen would swell again. In the case of two other patients, their abdomens were flat on arising in the morning, but after breakfast they swelled again.

We used progesterone in 5 cases, without benefit.

As these patients maintain a hard, rubbery abdomen, it is difficult to feel a pelvic mass. Under anesthesia, the examination may be done more properly. Usually after anesthesia, as noted by Biven, the abdomen would go down—and sometimes distend again immediately. We did not use any anesthesia.

DR. ROBERT SCHOBPACH: I am interested in the remark about the urinary bladder being distended; the condition has been noted in some cases. One worker suggested that there might be a spasm which prevented the urine from draining off. However, in most cases there has been no retention.

Concerning the occurrence of pseudocyesis in animals, the condition apparently is produced through the mechanism of the corpus luteum. Merely through stimulation of the cervix with a glass rod, pseudocyesis has been produced in animals and a corpus luteum discovered.

A number of patients were given injections, and only in the third, who had had psychotherapy, was the treatment successful in terminating the syndrome.

Again, I should like to emphasize that only superficial therapy was attempted and that the results were good, considering this. I do not feel that this syndrome was a deep or persistent one. We now have a few patients who are undergoing psychological studies.

Visceral Pain: Electrocerebral Shock Therapy as an Aid in Differentiating Structural and Psychological Causes, with a Report of Four Verified Cases. DR. JOSEPH C. YASKIN.

Organic disease sometimes eludes recognition even by most careful clinical and laboratory procedures. This is particularly true in the early diagnosis of visceral pain accompanied with psychological disturbances, which may vary in intensity from the *belle indifference* of the conversion hysteria through tension and anxiety to depression and agitation. When pain is due to organic causes, the accompanying psychological disturbances may represent (*a*) release phenomena of faulty personality integration, (*b*) coincidental affective reactions or (*c*) vague anxiety-depressive states, observed in diseases of the posterior part of the abdomen, and probably in other regions, but not related to personality makeup. When the internist is unable to find a satisfactory cause for the painful phenomena, he turns the patient over to the psychiatrist for treatment, and the psychiatrist is expected to assume that no organic disease exists. If the patient had marked depression, shock therapy is commonly considered a desirable procedure. I have observed four patients for whom the diagnosis of an organic disease was not established and who received electric shock therapy without procuring any relief from pain.

The first case was that of a woman aged 66 with pain in the left anterior side of the chest, of four years' duration, who proved to have a neurosarcoma of the rib. The second was that of a woman aged 50 with upper abdominal pain of several months' duration, who proved to have a tumor of the tail of the pancreas. The third was that of a man aged 60 with pain in the upper part of the abdomen of several months' duration. who proved to have a tumor of the middle of the pancreas. The fourth was that of a widow aged 42 who had had excision of a carcinoma of the rectum and who continued to have pain around the rectum and buttocks, who proved to have a recurrence of the tumor in the pelvis. In all these cases there were severe pain and considerable psychiatric disturbance, especially depression. All the patients received electric shock treatment to the point of being confused, without relief of pain.

Shock therapy was resorted to in these cases because of the inability of the clinician to diagnose organic disease and because they were characterized by psychological disturbances, which made the condition appear like an affective psychosis.

On the basis of the study of these four cases, attention is called to the fact that structural pain is accompanied with an appetite which is at its best in the morning and wanes as the day goes on, and that the reverse is true in the affective psychoses. It is concluded, on the basis of experience with these four cases, that shock therapy does not relieve structural pain and that the consulting psychiatrist must remain a good internist in order to avoid pitfalls in diagnosis and treatment.

DISCUSSION

DR. HARVEY BARTLE JR.: The second case Dr. Yaskin reported is my "skeleton in the closet." She came to me holding her hand to her abdomen. When the pain did not go away, I decided that something must be wrong. Even with known organic pain, one sometimes achieves dramatic results from a few shock treatments. When treatments did not relieve the patient, I had to look elsewhere for the cause of her pain.

All have seen cases of known organic disease with severe depression. In such cases should one use shock treatments to relieve the patient, or should one resort to an operation on the brain to give him a few more easy months? It is my feeling that severe depressions are uncommon in cases of known organic disease. Most such conditions are probably coincidental.

DR. HERBERT GASKILL: There are several points which I should like to make. First, we all need to be better internists in practicing psychiatry. During the past few years my colleagues and I have had many patients referred to us with pain for which no organic disease was found, and we have asked ourselves, "Is this functional, or has it an organic basis?" In trying to determine whether such pain is functional or organic, a few rules are to be remembered: First, it is not an "either/or" proposition; second, one can only try to evaluate the personality as one sees it. We can never have an absolute answer to some of these problems. It is impossible in some cases to determine whether the pain is functional.

These cases all presented difficult diagnostic problems. The organic pathologic process was extremely obscure. However, in these patients real depressions did appear to develop, as Dr. Yaskin was able to evaluate them. It would be my question: Should he have given electroshock treatments anyway in these particular situations?

Dr. Yaskin's patients had no functional pain during the period of blurring and had temporary remission of pain during electroshock.

Dr. Ewing, in Dr. Moore's service, saw a patient in January 1948 whose chief complaint was pain in the skin in the distribution of the right trigeminal nerve. His physician's diagnosis at that time was sinusitis. The pain was not relieved. His dentist found abscesed teeth, which were removed, with no relief of the pain. The patient was referred to the neurosurgical department of the University Hospital and was given an alcohol block, without relief. After that, he had avulsion of the root of the nerve. The pain persisted. It was then considered to be phantom pain. He was referred back for reevaluation. He was then mildly depressed and had suicidal thoughts. It became evident that a real personality change had occurred in the patient shortly before development of the pain syndrome. Dr. Ewing recommended electroshock therapy. Follow-up study shows that the patient has remained well and free from pain.

The third point I should like to make is the need of taking a careful history. Dr. Frazier and Dr. Spiller always took very careful histories and then tried to evaluate the history of the patient. Many a day I have heard them say that if one took more careful histories one would make fewer mistakes. In working with Dr. Alpers, I noticed that he always took very careful histories. A complete history is helpful in making differential diagnoses in such cases.

I would ask one question in regard to the third and fourth cases Dr. Yaskin reported: The psychological background is extremely important; was not the organic pathology an additional burden which precipitated the depression?

DR. JOSEPH C. YASKIN: I should like to add one or two words to what Dr. Bartle has said. We have one impression in common: If one knows there is organic disease with mental depression, should one use shock therapy? I doubt whether it is a good plan. I do not believe that shock therapy will relieve the pain. In these cases a lobotomy seems to be the procedure of choice. After such procedure, such patients do not complain much of pain and become dull enough not to mind the mental depression. I shall try this out as soon as I get a suitable case.

Dr. Gaskill asked me whether, as in case 3, that of a pancreatic tumor in a well known psychoneurotic, and in case 4, the physical factor was not enough to throw the patient into depression. It is quite possible that the physical disease acted as a precipitating factor of the depression in these cases.

Dr. Gaskill also reported a very interesting case of facial pain, the basis for which was presumably a powerful depression. This type is not as common as abdominal pain. My colleagues and I have reported a number of cases of pain in the face treated by all known methods which finally yielded to electroshock treatment. When pain is not readily diagnosable by known methods, it should always be evaluated in relation to a depressive state—which brings me right back to where I started 30 years ago.

Regular Meeting, April 8, 1949

Dynamics of Group Psychotherapy. DR. SAMUEL B. HADDEN.

In discussing the dynamics of group psychotherapy, it is proper to say that, although altered, all the dynamic forces inherent in individual psychotherapy are present in group psychotherapy and are, in some instances, intensified on a more effective plane. On entering a therapeutic group it is usual for a new patient to experience some anxiety, which may be compared analytically to the birth trauma. Shortly afterward a transference is established with the therapist, and soon identifications are made with other members in the group. These identifications may assume the proportions of actual transference, so that each individual may have some therapeutic effect on one or more members in the group. Catharsis is effective in the group, many times in a vicarious manner, as a patient who does not actively participate may so strongly identify himself with another patient whose problem is under discussion that it is in reality a discussion of his own problem. In this vicarious manner, the abreaction which the patient experiences may be more intense than in individual therapy.

In the group patients have a tendency to lose their feelings of isolation as they see others with similar problems and more quickly appreciate that their problem is understandable, and not a mystery to the physician. The multiple transferences which occur in the group may be shifting, so that the therapist may assume at times the aspect of the tolerant father or the critical mother, or vice versa. Various members of the group may be identified as siblings, and in the group the individual has the opportunity for greater reality testing. It has become my feeling that the therapy group is essentially an experimental setting in which the individual may obtain ego support, develop some modification of a too rigid superego and have the opportunity of an effective resocialization, as relationships which previously they were unable to maintain are effectively worked out in the group. As the patient finds acceptance and feels that he belongs in the group, his improved appreciation of reality may then be more easily carried into the community sector in which he is expected to function.

Experiences in Group Therapy Among Veterans. DR. SAMUEL A. ZERITSKY.

Religious establishments have been using a form of group experience for centuries. In 1905 Pratt established the class method of treating people with similar difficulties and found the technic more effective than individual discussions. After World War I, Simmel, a psychoanalyst, introduced group methods of inducing abreaction. Schilder, almost two decades later, published a series of papers revealing a psychoanalytical frame of reference in his group therapy sessions. Others, such as Slavson, began writing of activity group therapy, particularly with children, in which the dynamism of the method seemed to depend on social interaction. The orientational type of therapy within the group developed under military auspices during the recent war and included the exhibition of films and lectures by the leader. The tendency, however, in the majority of groups in present day civilian psychiatry, including the Veterans Administration, has been toward a nondirective role on the part of the therapist. Multiple interpersonal patterns within the group are created; a feeling of belonging develops, and improvement in social adaptation ensues.

Attendance at the sessions described in this paper are on a voluntary basis; the members are invited to join but are under no compulsion to accept. Their individual sessions are manifestly continued but in actuality are reduced both in frequency of appointments and in duration of the time allotted per session.

Theodore Dehne, M.D., *President in the Chair*

Regular Meeting, Feb. 10, 1950

Psychodiagnostic Drawing Test. DR. HERBERT FREED and JOYCE T. PASTOR.

The projective drawing technics of Machover and Buck were combined into a test in which the projections of both sexes, a house and a tree was utilized. It was theorized that in this way a study of both the body image and a potentially broader concept, the world image, was obtained. To the use of this procedure in the routine study of psychiatric entities, a research project on thalamotomies and hypothalamotomies was added. A series of drawings were

made by the patients before and after the operations. The tests were utilized not only to supplement the battery of psychological tests but also to determine the constancy of the body image when such vital areas of the brain as portions of the thalamus (the dorsal median nucleus) or of the hypothalamus were destroyed, the technic outlined in previous papers by Spiegel, Wycis and Freed being employed.

The authors concluded that there was a basic constancy in the drawings which were believed to portray the body image. The value of such a test in formulating the psychodynamics alone and in correlation with a battery of tests was discussed. It was felt that a further basis for study was afforded through the test material on patients in whom localized lesions involving the thalamocortical tracts were produced.

DISCUSSION

DR. THEODORE DEHNE: A great deal of interesting material has been presented this evening, much of it in an area where there is considerable conjecture. How one can separate what is obvious and meaningful from what has more the quality of fortuitousness is something one could discuss endlessly.

MR. MICHAEL DUNN: I am working on drawings of children. At Devereux (School) we have every conceivable type of psychiatric problem that could be found among children, and this paper brings up specifically several points of interest to me. At present I am collecting drawings from many children, normal children first. This is important, particularly as background for my comment on the courageous, though cautious, work Dr. Freed is doing. It is recognized that a drawing of a human being has exceptional value for the determination of the intellectual status of the person drawing the picture. This has been proved over the years.

I wish to pay credit to Dr. Goodenough, who in 1933 presented this technic. She could have been the leader of a productive movement in psychology; she sensed this but was unable to follow through.

Further development came as a result of the investigations of Schilder and his work in terms of the body image, the work of Freud and his concept of ego in relation to the body image and that of Rorschach in terms of projection of the body image.

Clinical Uses of and Evaluation of the Szondi Test. DR. MARGARET MERCER.

The Szondi test consists of 48 photographs of patients with mental disease, six under each of eight diagnostic categories. According to Szondi's theory, the personality disorders represented in the test are of genetic origin, and the subject's emotional reactions to these photographs were believed to depend on some similarity between the gene structure of the patient represented by the photograph and that of the subject reacting to the photograph. Biologists do not agree with Szondi's theories of heredity. A number of students have pointed out that his conclusions can be justified by a psychoanalytic explanation. The six sets of eight photographs are presented one after the other, and the subjects choose the two most liked and the two most disliked photographs of each set. These 24 choices are recorded in a profile. At least six such profiles are obtained.

The test is easy to administer but is difficult to interpret. It can easily be misused in the hands of a person not adequately trained in its use. Until recently, its use in the United States was limited by the fact that all publications concerning it were Hungarian or German. Since World War II, some of Szondi's students have come here, and instruction in the method is becoming available. The outstanding person in this group is Dr. Susan Deri, who has recently published an exposition of the dynamic thought processes in the interpretation of the test which is consistent with the psychoanalytic formulations.

The clinical psychology service at the Veterans Administration Hospital at Coatesville, Pa., with the cooperation of the psychiatric staff, has been studying this test for more than a year. Whether or not one accepts Szondi's rationale or the psychoanalytic explanations of why the test works, it has proved itself empirically to be a useful projective technic.

DISCUSSION

MR. S. M. RAPPAPORT: As Dr. Dehne mentioned, I have been experimenting with the Szondi test clinically for some time. I do not profess to be an expert in its use and cannot set myself

up as a critic of Dr. Mercer's excellent paper. I have, however, a few remarks on the evaluation of the clinical use of the Szondi test. In the field of psychology many years ago crucial experiments were made which may be evaluated in the light of Szondi's work. The subject was asked to judge the expression of a photograph. It was found conclusively that it is impossible to determine the emotional expression of another person when shown in a photograph. This leads us to the question of whether we can accept the theory of Szondi, which utilizes the concepts of accurate evaluation and the expression of fear. The entire test is based on factoral association. In using this, the subject is asked to associate to a photograph presented to him. One finds that the conscious verbalizations of the subject seem to tie in rather well with the underlying emotional problem of the subject. The lack of publicly observable data is an important restriction to the use of the Szondi test at this time.

DR. OLIVE MORGAN: My associates and I find this test exceedingly valuable in combination with the other tests in the battery. We find that it does not always contribute material consistent with the other tests. We are trying to check those instances in which it does not seem to hold up, and we find it is usually with patients who are seriously disturbed or are hostile and reject the whole idea. We have tried giving the test to a number of medical students, many of whom are hostile to the idea and look on it as a time waster. We feel that a tremendous amount of work has to be done with it to provide a statistical basis for some of the assumptions made. One disadvantage of the test is that people have to come a number of times to take the test, and that is sometimes rather difficult.

DR. HERBERT FREED: One may as well admit that the projective technics are the bastard offspring of psychiatry and psychology. We psychiatrists should take the bastard in out of the cold. It is just as great a scientific crime not to understand these tests as it is not to utilize them with clinical investigations and observations. Most psychiatrists are failing in their duty when they do not try to understand them.

PHILADELPHIA NEUROLOGICAL SOCIETY

Helena E. Riggs, M.D., *Presiding*

Regular Meeting, Feb. 3, 1950

Dissimilar Lesions of the Nervous System in the Same Patient: Parasagittal Meningioma and Syringomyelia. DR. WILLIAM KAELBER, Rochester, N. Y. (by invitation).

The case reported is that of two independent lesions of the nervous system in the same patient, one being a parasagittal meningioma and the other true syringomyelia. This situation presented considerable diagnostic difficulty, which was in part solved by the findings in the electroencephalogram and pneumoencephalogram; but other features remained obscure until revealed by autopsy. The syringomyelic lesion was of considerable length, extending from the middle of the medulla to the sacral portion of the spinal cord.

A review of the literature demonstrated, among other things, that only one case of syringomyelia with a brain tumor (of the glioma group) had been reported since 1940. It was also noted that the cerebral neoplasm in the present case was of mesodermal origin.

DISCUSSION

DR. ANTHONY TORNAY: When my colleagues and I first examined this patient, he had evidence of lower motor neuron disease in the lower extremities, pronounced horizontal and vertical nystagmus and marked mental dulness. He therefore had evidences of multiple lesions in the nervous system. He was also a known alcoholic. It is important to point out that just prior to operation he appeared to go into shock. This lasted only several hours, and he seemed to recover completely. Air studies localized one of the lesions in the nervous system. We were surprised by the size of the tumor. We did not suspect the syringomyelia, which was found at autopsy.

DR. MICHAEL SCOTT: When I saw this patient prior to operation, the most interesting manifestation was the foot drop, without increased reflexes and the Babinski sign.

We found a tremendous lesion, and it was necessary to ligate the middle third of the sagittal sinus. We were thus able to remove the entire tumor. However, in view of the

circumstances, it would have been better to leave a small portion of the tumor, for it was probably slow growing and the patient might have lived a number of years.

The Hypothalamic Syndrome: Report of a Case. DR. PETER SAYERS (by invitation), DR. HENRY A. SHENKIN and DR. JOSEPH C. YASKIN.

Lesions confined to the anatomic limits of the hypothalamus cerebri are extremely unusual. After a brief discussion of the recent advances in knowledge of the anatomy and physiology of this region, the authors presented the case of a previously healthy woman aged 29, the mother of six children, in whom over a period of three years there had progressively developed convulsions, protracted fever with chills, generalized weakness and fatigue, personality change with loss of all sense of responsibility, increased appetite and gain in weight in spite of fever, loss of libido, a phase of diabetes insipidus, amenorrhea, involuntary autonomic discharges, sham rages and unilateral papilledema, due to infiltration of the left optic nerve.

Necropsy revealed a clearly defined granulomatous lesion entirely within the hypothalamus, with no encroachment on surrounding structures. Microscopically, the lesion strongly resembled Hodgkin's disease.

It was particularly emphasized that lassitude, irresponsibility and bulimia (the prefrontal lobotomy syndrome) and the unpredictable fight and flight reactions so frequently attributed to interruption of fibers from the dorsomedial nucleus of the thalamus may be produced by lesions confined to the ventral portion of the diencephalon.

DISCUSSION

DR. GEORGE GAMMON: May I ask Dr. Sayers what were the nature of the convulsive manifestations that this woman had and whether there were many of them?

DR. HELENA E. RIGGS: Dr. Sayers showed me his slides this week, and they were very similar to those in a case at Philadelphia General Hospital about three years ago; only in our case the diagnosis was much easier because the patient had xanthomatous nodules in the skin. The woman had been treated with posterior pituitary U. S. P. for diabetes insipidus for three years. Her weight had increased from 105 to 185 pounds (47.6 to 83.9 Kg.) in a few months. She was extremely somnolent. She had uncontrollable diabetes insipidus and had had amenorrhea for several days. Necropsy showed a lesion very much in the same location as that in Dr. Sayers' case except that it included the infundibular stalk. It was bright butter yellow and looked like fat. There were a number of lesions of the same type throughout the body. Dr. William Ehrich and I considered the case one of Christian-Schüller disease in a young adult and felt that the hypothalamic symptoms were explainable not so much by the type of lesion as by its location.

DR. PETER SAYERS: In answer to Dr. Gammon's question, the seizures occurred 2½ years before the patient was seen clinically and the history was very hazy, but apparently they were grand mal seizures. Unless these convulsions can be related to Jasper's recent paper on seizures from the massa intermedia, I cannot explain them.

Clinical Evaluation of Mesantoin® in Treatment of Epilesy. DR. AARON W. MALLIN and DR. GEORGE D. GAMMON.

Mesantoin® (methyl phenylethylhydantoin) therapy, given to 40 patients with convulsive states of long duration and inadequately controlled by other treatment, effected considerable improvement. Thirty-seven per cent were free of attacks for periods of three to 18 months, and 40 per cent had a considerable reduction in frequency of attacks; a total of 87 per cent were improved. On the other hand, 18 per cent had no or only slight reduction in frequency, and 5 per cent were worse while under therapy.

Hypertrophy of the gums from diphenylhydantoin disappeared in two persons when mesantoin® was substituted for the drug, as did severe prolonged ataxia in one case. Toxic reactions occurred in one-half the patients but were mild in most and disappeared in many despite continued therapy. The potential danger of granulocytopenia is evident, for one patient succumbed—the fourth reported case of this complication.

The results were obtained by substituting mesantoin® for diphenylhydantoin in combination with other current therapy. No comparison of effectiveness on similar dose levels was attempted.

In this drug one has another agent which is most effective in control of motor seizures but which must be employed with full realization of its toxic potentialities.

DISCUSSION

DR. GEORGE GAMMON: These results simply confirm several published reports on the effectiveness of this drug. We were disturbed to encounter the complication of fatal granulocytopenia.

The toxic reactions of these hydantoin compounds are best understood from a study of nirvanol® (phenylethylhydantoin), formerly employed in the treatment of rheumatic fever, and subsequently of rheumatic chorea. It regularly produced a rash, fever and a drop in the leukocyte count. This reaction was thought to have something to do with its efficacy in therapy. Its use in chorea was abandoned because of the production of hemorrhagic encephalitis.

DR. FRANCIS FORSTER: We at the epilepsy clinic at Jefferson Medical School Hospital have become wary of mesantoin.® We have had two fatalities from aplastic anemia and one case of severe jaundice.

The monthly blood count is usually an adequate safeguard. Occasionally, however, it is not. A patient who was followed with monthly blood counts maintained the leukocyte count very well; then, in the interval of one month, it dropped, and the patient died in the hospital of aplastic anemia.

DR. MATTHEW T. MOORE: In my experience mesantoin® has been an effective drug in the control of grand mal seizures. However, I have had several cases in which the toxic reactions were alarming and severe. In two cases there developed an acute scarlatiniform rash with sore throat, which required hospitalization, two weeks after medication had been started. In a third case a similar reaction developed two months after completion of mesantoin® therapy. In a fourth case a rash developed, and use of the drug was discontinued in favor of diphenylhydantoin sodium; but, owing to hypertrophy of the gums, the patient was again given mesantoin.® Within three days a pronounced eczematoid rash developed over both legs; this was followed by deep, crater-like ulcerations with surrounding areas of tissue gangrene. When use of the drug was discontinued and antihistaminics were given, the disorder cleared within several weeks. In still another case a mild flush, diffusely distributed, developed while the patient was taking 1½ grains (0.097 Gm.) three times daily at the outset. Reducing the dose considerably and gradually building it up to the effective dose created a tolerance, without return of the rash.

DR. SHERMAN F. GILPIN JR.: In the discussion of toxic reactions to administration of mesantoin,® I have not heard sufficient emphasis on one type of reaction which my colleagues and I have observed at the neurological clinic of the Temple University School of Medicine. I refer to the combination of high fever, sore throat and a cutaneous rash, which looks very much like that of scarlet fever. It seems to me that this reaction could be confused with scarlet fever.

At Temple University we experienced difficulty in keeping some of our patients on mesantoin® because of other toxic reactions, in particular, sleepiness and headache. The somnolence was made worse when phenobarbital was given with the mesantoin,® and we had some difficulty in convincing the manufacturer that the two drugs should be dispensed separately.

DR. AARON MALLIN: I should like to add a word about the case of death from aplastic anemia. The patient was very close to death several times before the final episode, the nearness to death being unrelated to mesantoin® therapy. She had had high fever (infections) on many occasions, and frequent telephone calls from her physician indicated her proximity to death.

I also want to emphasize that the blood counts were normal until the final illness, and seizures were completely controlled for 13 months prior to death.

Petit Mal Epilepsy Occurring in Status. DR. FRANCIS M. FORSTER and DR. WEIR M. TUCKER.

Repeated generalized convulsions, or status epilepticus, is a well known clinical condition. Petit mal status is less widely known and may offer a difficult problem in differential diagnosis,

especially when the petit mal attacks are of the short, staring type. Two cases of petit mal status were presented. In the first the clinical picture during petit mal status was difficult to differentiate from psychomotor epilepsy and from a psychoneurotic depression. In the second case it was difficult to differentiate clinically between petit mal status and psychomotor seizures. The difficulties in clinical differentiation were discussed, and the importance of electroencephalography was stressed.

DISCUSSION

DR. CHARLES RUPP JR.: I should like to ask Dr. Forster how he would differentiate pyknolepsy and these conditions which he has just described.

DR. GABRIEL SCHWARZ: For the past few years, my colleagues and I have been following 15 children at the University of Pennsylvania who have what is called status epilepticus, petit mal type. They were thought to be feebleminded. They had no grand mal seizures. There was little clinical evidence that they had the convulsive state. The electroencephalograms showed almost continuous high voltage spike and dome wave or slow wave pictures.

Some of these children we have followed over many years. A number of them have been placed under trimethadione (tridione®) or diphenhydramine therapy. Their apparent mental retardation has altered favorably.

DR. FRANCIS M. FORSTER: In answer to Dr. Rupp's question about pyknolepsy: I do not think pyknolepsy is different from epilepsy.

Recently we treated a woman for grand mal seizures, and when we asked about a history of short stares she denied having had them.

When she came back the next week, she said, "When I was a little girl Dr. Dercum used to show me off to the medical students here at Jefferson because I used to black out a bit." When she was a little girl she had had pyknolepsy, and when she grew up she had major attacks.

Thank you, Dr. Schwarz, for emphasizing again the importance of this condition. Certainly, when these patients are out of contact they cannot be at their best intellectual level.

SPECIAL NOTICE

For the general information of indexers, catalogers and library personnel with reference to the listing of the new title of this journal, we advise that the *Quarterly Cumulative Index Medicus* policy be followed. The *Quarterly Cumulative Index Medicus* with its volume 49 (January-June 1951) will list this journal under the new title, so that the letters A. M. A. will be included as an integral part of the title. For the completion of volume 48 (July-December 1950) the *Quarterly Cumulative Index Medicus* will continue to use the old title, without adding the designation A. M. A.

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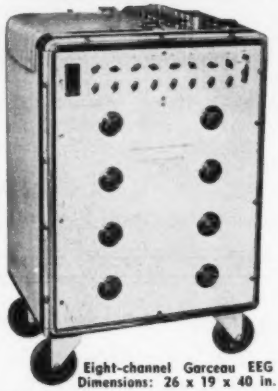

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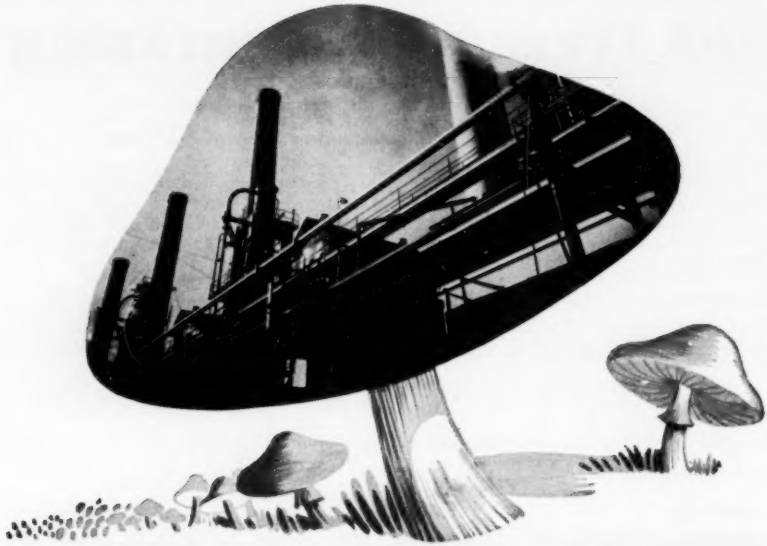

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